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volume I

Edited by
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Telemedicine in neurology, volume I: In neuro-otology, neuro-ophthalmology, and movement disorders patient care and treatment

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STUDY PROTOCOL
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Study Protocol for the Development of a European eHealth Platform to Improve Quality of Life in Individuals With Huntington's Disease and Their Partners (HD-eHelp Study): A User-Centered Design Approach

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Background: Huntington's disease (HD) is an autosomal dominant neurodegenerative disease that affects the quality of life (QoL) of HD gene expansion carriers (HDGECs) and their partners. Although HD expertise centers have been emerging across Europe, there are still some important barriers to care provision for those affected by this rare disease, including transportation costs, geographic distance of centers, and availability/accessibility of these services in general. eHealth seems promising in overcoming these barriers, yet research on eHealth in HD is limited and fails to use telehealth services specifically designed to fit the perspectives and expectations of HDGECs and their families. In the European HD-eHelp study, we aim to capture the needs and wishes of HDGECs, partners of HDGECs, and health care providers (HCPs) in order to develop a multinational eHealth platform targeting QoL of both HDGECs and partners at home.

Methods: We will employ a participatory user-centered design (UCD) approach, which focusses on an in-depth understanding of the end-users' needs and their contexts. Premanifest and manifest adult HDGECs ($n = 76$), partners of HDGECs ($n = 76$), and HCPs ($n = 76$) will be involved as end-users in all three phases of the research and design process: (1) Exploration and mapping of the end-users' needs, experiences and wishes; (2) Development of concepts in collaboration with end-users to ensure desirability; (3) Detailing of final prototype with quick review rounds by end-users to create a positive

user-experience. This study will be conducted in the Netherlands, Germany, Czech Republic, Italy, and Ireland to develop and test a multilingual platform that is suitable in different healthcare systems and cultural contexts.

Discussion: Following the principles of UCD, an innovative European eHealth platform will be developed that addresses the needs and wishes of HDGECs, partners and HCPs. This allows for high-quality, tailored care to be moved partially into the participants' home, thereby circumventing some barriers in current HD care provision. By actively involving end-users in all design decisions, the platform will be tailored to the end-users' unique requirements, which can be considered pivotal in eHealth services for a disease as complex and rare as HD.

Keywords: Huntington disease, neurodegenerative diseases, telemedicine, eHealth, user-centered design, quality of life, study protocol, tele-neurology

GENERAL INFORMATION

Protocol Title

Development of an eHealth care model to improve quality of life in Huntington's Disease: a user-centered design study (HD-eHelp).

Research Sites and Investigators

Research sites from the Netherlands, Germany, Czech Republic, Italy, and Ireland will be involved in this study. **Table 1** provides an overview of the participating research sites and investigators within the European eHealth Care Model for Rare Neurodegenerative Diseases (HEALTHE-RND) consortium.

Study Status

At time of submission of this manuscript, the study status is recruiting.

INTRODUCTION

Huntington's Disease (HD) is a rare, autosomal dominant neurodegenerative disease characterized by progressive motor symptoms, cognitive impairments, and neuropsychiatric symptoms (1, 2). The disease is caused by a cytosine-adenine-guanine (CAG) repeat expansion in the *huntingtin* (HTT) gene (1). Reduced penetrance is seen in individuals with 36–39 CAG repeats, whereas individuals with >39 repeats will develop HD (1). HD affects an estimated 10.6–13.7 per 100,000 individuals in Western populations (3). Children with an HD affected parent have a 50% risk of inheriting the HD gene expansion. Clinical symptom onset is preceded by the premanifest stage (including the pre-symptomatic and the prodromal phase) (4, 5), in which subtle motor, cognitive and/or neuropsychiatric symptoms can already occur up to 10–15 years prior to the start of clear motor signs (4–6). After the onset of clinical motor changes (1, 6), which is still the "landmark" for manifest disease, life expectancy ranges between 15 and 20 years (2).

Disease onset usually occurs in the fourth or fifth decade of life (2, 6), when individuals are often very active in work, family and social life. As the disease progressively affects various functions essential for participation in everyday life activities, individuals become more dependent over time and the need for (long-term) care increases (1, 6). As no cure is available to date, current treatment strategies focus on symptom management and quality of life (QoL) maintenance (1, 3, 7). Previous studies have shown that HD greatly impacts the QoL of HD gene expansion carriers (HDGECs) (3, 8–10), even prior to symptom onset (3, 9). QoL tends to decline as the disease progresses over time (9, 11, 12), with individuals in the advanced stage often experiencing a worse QoL as compared to individuals at risk or in the premanifest stage (9, 11, 12). Partners of HDGECs also experience impaired QoL (13–15), especially with regard to coping, financial expenses, gaining access to care services, and perceived lack of knowledge from healthcare providers (HCPs) (13).

Due to the complex clinical nature of HD, there is an increasing need for comprehensive and multidisciplinary care services (16, 17), ranging from advice about genetic testing to palliative care. Although several HD expertise centers have been established across Europe (2, 18, 19), these specialist services often serve large geographical areas. Moreover, these services are not always instantly available, accessible or in close proximity to those seeking care (18). Other barriers impeding HD care provision include health care and transportation costs (2, 18). In addition, increasing physical limitations and burden, especially in the later stages of the disease, might pose difficulty in seeking and accessing care, leaving those with the greatest care need receiving the least care (20). To overcome these barriers, delivery of expert care should transcend geographical borders. More importantly, specialized professional care should be arranged and provided in such a way that HDGECs can live at home as long as possible while maintaining acceptable QoL. This results in the need for innovative ways to facilitate QoL maintenance in the home situation, primarily by increasing access to specialized professional care regardless of distance to care centers.

Abbreviations: HD, Huntington's disease; HTT, *huntingtin* gene; CAG, cytosine-adenine-guanine repeat length; QoL, quality of life; HDGECs, Huntington's Disease gene expansion carriers; HCP, health care providers; PD, Parkinson's Disease; UCD, user-centered design; preHD, premanifest HDGECs; mHD, manifest HDGECs; FPEP, Family Patient Expert Panel; UHDRS, Unified Huntington's Disease Rating Scale; eCRF, electronic case report form.

TABLE 1 | Research sites and investigators involved in the study.

Investigators	Role	Research site
The Netherlands		
P. J. C. van Lonkhuizen, MSc	Coordinating investigator	LUMC*, Topaz, NeLL
N. J. H. Vegt, PhD	Co-investigator	LUMC*, NeLL
E. Meijer, PhD	Co-investigator	LUMC*, NeLL
A. Heemskerk, PhD	Co-investigator	LUMC*, Topaz
E. van Duijn, MD, PhD	Co-investigator	LUMC$^{\$}$, Topaz
S. T. de Bot, MD, PhD	Co-investigator	LUMC$^{\nabla}$
N. H. Chavannes, MD, PhD	Principal investigator	LUMC*, NeLL
Germany		
G. B. Landwehrmeyer, MD, PhD	Principal investigator	University Hospital Ulm
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W. Frank, MSc	Coordinating investigator	University Hospital Ulm
R. Hoffmann, MD	Co-investigator	University Hospital Ulm
Czech Republic		
J. Klempíř, MD, PhD	Principal investigator	Charles University Prague
K. Dolečková, MD	Co-investigator	Charles University Prague
O. Klempířová, PhD	Co-investigator	Charles University Prague
O. Ulmanová, MD, PhD	Co-investigator	Charles University Prague
J. Roth, MD, PhD	Co-investigator	Charles University Prague
Italy		
F. Squitieri, MD, PhD	Principal investigator	IRCCS Casa Sollievo della Sofferenza Hospital
S. Maffi, MSc	Coordinating investigator	IRCCS Casa Sollievo della Sofferenza Hospital
E. Scaricamazza, MD, PhD	Co-investigator	IRCCS Casa Sollievo della Sofferenza Hospital
S. Migliore, PhD	Co-investigator	IRCCS Casa Sollievo della Sofferenza Hospital
M. Casella, MSc	Co-investigator	Italian League for Research on Huntington
Ireland		
J. Hoblyn, MD	Principal investigator	Bloomfield Hospital, Trinity College Dublin
M. Thangaramanujam, MISCP	Coordinating investigator	Bloomfield Hospital, Trinity College Dublin

LUMC, Leiden University Medical Center; Topaz, Huntington Center Topaz Overduin; NeLL, National eHealth Living Lab; IRCCS, Istituto di Ricovero e Cura a Carattere Scientifico.
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eHealth provides promising opportunities to facilitate such care, as it delivers and/or enhances health care services by using information and communication technologies (21). eHealth offers many possibilities, including home-based monitoring of health parameters, remote treatment options, as well as communication and information exchange between patients, family members and HCPs (20, 22). In addition, eHealth can increase care capacity by connecting experts to local clinicians remotely (20). Most importantly, eHealth allows for personalized, tailored care to be moved partially away from highly specialized centers (requiring patients to travel) into the patients' home (20, 22), which can be considered paramount for a disease as complex and rare as HD.

Although eHealth is considered promising in terms of acceptability, feasibility and effectiveness in other neurological and neurodegenerative diseases [e.g., dementia, Parkinson's disease (PD), multiple sclerosis] (23–30), research on eHealth (development) in HD is limited (31–35). A small-scale pilot study conducted in the Netherlands showed that an interactive knowledge website for HD patients and caregivers, combined with a videoconferencing tool (iQare), increased continuity of care as well as the quality of contacts between patients and informal/professional caregivers, without any travel time (31). eHealth was also found to be useful in conducting remote motor assessments and predictive testing services in HD (32–34), while maintaining quality of care and support (33).

In spite of the rapid growth in eHealth services more generally, (long-term) uptake of these services is often poor (36, 37) due to limited integration into the clinical workflow, reimbursement and legislation issues, and privacy and security issues (37–39). Limited uptake is also related to not actively involving end-users (e.g., patients) in an early stage of the design and development process (22, 37, 39). This may result in a lack of functionalities that are desired from a user perspective as well as in poor usability and user experience (37, 38, 40–42). Additional challenges in eHealth development reported in other neurodegenerative diseases, including PD, are the strong focus on motor aspects of the disease as opposed to important sources of

disability reported by patients (e.g., depression, fatigue, and sleep disturbances), and the lack of user engagement (27, 29, 30).

A user-centered approach, in which end-users are closely involved in the design process, is therefore desired. It is assumed that this will lead to the necessary insight for developing eHealth that facilitates the patients' QoL, given its suitability as shown in other neurological and neurodegenerative diseases (43–47). Actively involving both HDGECs and their partners, and addressing their needs is important especially in HD given the complexity and diversity of symptoms and the variety in needs experienced in different stages of the disease, including pre-symptomatic and prodromal stages. In addition, partners of HDGECs often have the tendency to neglect their own experiences and needs (15), yet these should not be overlooked. As a high level of unmet needs for health and social services can negatively impact health-related QoL in HD (12), it is important to include the needs of both HDGECs and their partners in the development of eHealth technologies. By also actively involving HCPs with expertise in HD, disease-specific characteristics, in particular neuropsychiatric and cognitive impairments (18), can be considered in advance in the eHealth development process.

To date, no HD-specific needs assesment exists in relation to QoL from the perspective of HDGECs and their partners. To ensure high-quality remote care services that increase the QoL of HDGECs and their partners across Europe, it is therefore paramount to include the perspective of HDGECs, their partners and HCPs in designing and developing an eHealth platform. A participatory user-centered design (UCD) approach ensures the inclusion of these perspectives by closely involving end-users in the development process, thereby increasing the probability of a good fit between the eHealth platform and end-users' needs, wishes, and daily activities (39, 48, 49). In the present study we will use the principles of UCD to develop an innovative eHealth platform to facilitate QoL in HDGECs and partners across Europe. This may be digital information solutions (e.g., websites, apps, online videos), digital communication tools (e.g., sensors, questionnaires, chat messaging), and/or digital support tools (e.g., shared agendas, notification systems). In this article we outline a detailed description of the aim, design and study procedures of the HD-eHelp study.

Study Aim and Objectives

The HD-eHelp study aims to capture the needs and wishes of HDGECs, partners and HCPs in order to develop a European eHealth platform following the principles of UCD (48). The specific study objectives are, to:

1) explore and map desires, needs and experiences of HDGECs, partners, and HCPs in relation to QoL, HD care and eHealth;
2) identify eHealth opportunities and strategies to fulfill these desires and needs;
3) identify design requirements for an eHealth platform in collaboration with end-users to ensure desirability, and;
4) develop prototypes of the eHealth platform with end-users to create a positive user-experience.

METHODS AND ANALYSIS

Study Design

We will employ a UCD approach (48) in which an understanding of the end-users' needs, preferences and contexts is pivotal. In our study, we will include HDGECs, partners and HCPs as end-users. To optimally align the eHealth platform with their needs and wishes, end-users will participate in all three phases of the research and development process (i.e., 1. Exploration; 2. Concept development; 3. Prototype testing). As user-centered (participatory) design approaches have not been extensively used or described in HD (34, 50), we provide a detailed description of how we adjusted this approach to the multiple target groups and multinational nature of our study in the procedure section.

This study will be coordinated from the Netherlands. Research sites from the Netherlands, Germany, Czech Republic, Italy, and Ireland (see **Table 1**) will be involved to develop and test a multilingual platform that is suitable within different healthcare systems and cultural contexts. The duration of the study will be ∼18 months, including preparation, data analysis and prototype development. A large-scale evaluation of the platform in a randomized controlled trial (RCT) is scheduled, yet beyond the scope of this study protocol.

Study Sample and Recruitment

Premanifest (preHD) and manifest (mHD) gene expansion carriers who are living at home, partners of HDGECs, and HCPs will be invited to participate in this study. **Table 2** provides an overview of the eligibility criteria for each participant group.

We aim to recruit HDGECs from the locally held Enroll-HD database (https://www.enroll-hd.org/) at the respective research sites (51). Enroll-HD is a global, on-going observational study for families affected by HD, collecting longitudinal data on disease characteristics and progression (51). With over 20,000 participants enrolled worldwide, Enroll-HD provides a large database of HDGECs for which phenotype and genotype are well-established, providing additional context for mapping their desires and needs across different disease stages in this study. HDGECs are not required to have a spouse/partner to participate in this study and will be selected to cover a wide range of disease stages.

Partners (i.e., spouses or unregistered/unmarried partners of premanifest and manifest HDGECs) and HCPs will be recruited from clinics, HD centers, patient groups and via the research sites' primary and secondary care networks in the respective countries. The HCP sample will represent professionals who work in HD expertise centers and will be selected to cover all major expertise that is involved in HD care (e.g., neurologists, psychiatrists, psychologists, social workers, speech and swallowing therapists, dieticians, occupational therapists, and physiotherapists).

Potentially eligible participants will be informed about this study (face-to-face or by telephone) by the coordinating researcher(s) at each site and will receive a study information package, if interested. After a minimum period of 7 days, HDGECs will be contacted again and provided with additional information or clarification, if needed. Partners and HCPs can indicate their interest in participation via a response card. Participants will be invited to the first study activity upon receival

TABLE 2 | Eligibility criteria for study participants.

	Inclusion criteria	Exclusion criteria
HDGECs	• Genetically confirmed HD (i.e., CAG ≥ 36) • No clinical motor features (i.e., UHDRS DCL < 4) in case of premanifest HDGECs. Clinical motor features (i.e., UHDRS DCL = 4) in case of manifest HDGECs • Age ≥ 18 years • Living at home • Proficient in language of respective country • Current participation in Enroll-HD • Ability to attend study sessions	• Having a partner that participates in this study • Being a FPEP member of this study • Any present serious psychiatric, neurological, sensory, or any other comorbid disorders known to influence participants' judgements and therefore likely to affect the needs and desires experienced as well as the ability to assess eHealth use (as judged by clinical team) • Inability to give consent
Partners	• Spouse or partner of premanifest or manifest HDGECs • Living together with premanifest or manifest HDGECs • Age ≥ 18 years • Proficient in language of respective country • Ability to attend study sessions	• Being an HDGECs themselves (as confirmed by genetic test) • Having a partner that participates in this study • Being a FPEP member of this study • Any present serious psychiatric, neurological, sensory, or any other comorbid disorders known to influence participants' judgements and therefore likely to affect the needs and desires experienced as well as the ability to assess eHealth use (as judged by clinical team) • Inability to give consent
Health care providers	• Providing HD care ≥ 2 years • Age ≥ 18 years • Proficient in language of respective country • Ability to attend study sessions	• Inability to give consent

HDGECs, Huntington's Disease gene expansion carriers; HD, Huntington's Disease; CAG, cytosine-adenine-guanine repeat length; UHDRS, Unified Huntington's Disease Rating Scale; DCL, Diagnostic Confidence Level; FPEP, Family Patient Expert Panel.

of the signed informed consent forms. All participants will receive travel reimbursement, if applicable.

Sample Size

We estimated the number of participants based on guidelines for user testing (52), thereby correcting for anticipated attrition rates. Five participants generally find 80 percent of all problems when testing a moderately complex concept or prototype. This is more than enough for developing an eHealth platform that can be tested in an RCT. However, as the target users (i.e., patients and partners) of the intended eHealth platform are experiencing very diverse stages of the disease, we include at least 7 participants per stage (i.e., preHD or mHD) per target group. The study design allows participants to take part in multiple phases. If they are unwilling or unable to participate in subsequent phases, additional participants will be recruited until data saturation (i.e., no new insights emerging from newly collected data) is reached within each study phase (53).

Table 3 provides the estimated number of participants per phase and per country throughout the study. In total, we aim to include 20 HDGECs (10 preHD; 10 mHD), 20 partners (10 of preHD; 10 of mHD) and 20 HCPs in the Netherlands. In Germany, Czech Republic, Italy, and Ireland we aim to include 14 HDGECs (7 preHD; 7 mHD), 14 partners (7 of preHD; 7 of mHD) and 14 HCPs per country. This will result in the inclusion of 76 HDGECs (38 preHD; 38 mHD), 76 partners (38 of preHD; 38 of mHD) and 76 HCPs throughout the whole study.

Study Procedures

The different study procedures for each UCD phase, and how we adjusted these to the multinational nature and target groups of our study, are described in detail below. As the study is coordinated from the Netherlands, Dutch end-users will be involved in all phases of the development process. Due to feasibility and time constraints, end-users in the other participating countries will only be involved in phase 1 and 3 (see **Table 3**). This is considered sufficient to design and adapt the eHealth platform to each language and healthcare system. To prevent a loss of lingual and cultural aspects in concept development during phase 2, the international project team and an international Family Patient Expert Panel (FPEP) will be actively involved throughout phase 2. The panel consists of one representative from each participating country, appointed by the respective national HD association. In addition, two people from the patient advocacy group in the European Reference Network for Rare Neurological Diseases participate to have additional disease groups represented.

Throughout the study, regular meetings with the international project team, a Dutch advisory board of HCPs and the FPEP will provide guidance to the research and design process. The HCP advisory board and the FPEP will review study procedures and materials to ensure suitability and comprehensibility. Prior to the start of the study in each country, all relevant study materials will be translated into the respective languages. Guidelines for all study sessions have been developed. Study sessions will be audio recorded and conducted by trained staff.

Phase 1: Exploration

We will gather an in-depth understanding of end-users' needs, desires and experiences regarding QoL, HD care, and eHealth possibilities using interviews and generative techniques. As compared to more conventional qualitative techniques (i.e.,

TABLE 3 | Estimated number of participants per UCD phase per country.

	NL	GE	CZ	IT	IE	Total
PHASE 1: EXPLORATION						
Interviews						
HDGECs						**36**
preHD	6	3	3	3	3	
mHD	6	3	3	3	3	
Partners						**36**
preHD	6	3	3	3	3	
mHD	6	3	3	3	3	
Focus groups						
HCPs	12	6	6	6	6	**36**
Total phase 1	**36**	**18**	**18**	**18**	**18**	**108**
PHASE 2: CONCEPT DEVELOPMENT						
Co-creation sessions	*	–	–	–	–	*
Concept testing	*	–	–	–	–	*
Total phase 2	*	–	–	–	–	*
PHASE 3: PROTOTYPE TESTING						
Prototype testing	*	–	–	–	–	*
"Think-aloud" sessions						
HDGECs						**40**
preHD	4	4	4	4	4	
mHD	4	4	4	4	4	
Partners						**40**
preHD	4	4	4	4	4	
mHD	4	4	4	4	4	
HCPs	8	8	8	8	8	**40**
Total phase 3	**60**	**24**	**24**	**24**	**24**	**156**
Study total	**60**	**42**	**42**	**42**	**42**	**228**

*UCD, User-centered design; NL, the Netherlands; CZ, Czech Republic; GE, Germany; IT, Italy; IE, Ireland; HDGECs, Huntington's Disease gene expansion carriers; preHD, premanifest HDGECs; mHD, manifest HDGECs; HCPs, health care providers. *In the Netherlands, the same individuals that participated in the exploration phase (phase 1) will be asked to participate during co-creation and concept testing (phase 2), and prototype testing (phase 3). The bold values were meant to highlight the total sample size (as the bold values are the sum of the sample sizes of each individual study group).*

interviews and focus groups), generative techniques (54), such as sensitizing assignments and journey mapping, can help to facilitate a deeper level of understanding (55) and access people's tacit knowledge (i.e., easy to act upon but difficult to express in words) and latent knowledge (i.e., not yet aware of) (56). As desires, needs and experiences are often concealed in these deeper levels of knowledge, these techniques provide access to the user's hidden world (55) and at the same time help to build empathy during the design process (57).

All participants will complete a workbook consisting of sensitizing assignments that encourage them to reflect on their routines, habits and feelings regarding HD and QoL (e.g., current/future complaints, important conversations and locations, housing situation and tools used, reflection of a day in their lives). This awareness helps to express their experiences and needs during semi-structured interviews (in case of HDGECs and partners) and focus groups (in case of HCPs). Participants will be asked to complete an assignment every day (∼10 min per day) for a total of 7 days at home (HDGECs/partners) or at work (HCPs). Participants can receive daily reminders by phone/e-mail upon request. The sensitizing assignments have been co-developed with the HCP advisory board/FPEP and have been adapted and tailored to each participant group. To ensure suitability and comprehensibility, the assignments for HDGECs were pilot tested with one premanifest and one manifest HDGEC (and spouse). This resulted in some important adjustments for the workbooks for manifest HDGECs, including for example landscape instead of portrait orientation, larger font size, more writing space, and less suggestive examples to avoid copying (see **Figure 1** for an example of an assignment in the workbook for manifest HDGECs). Together with the researchers from the respective sites, the final workbooks were adapted to each language.

The interviews with HDGECs and partners are aimed at understanding participants' daily experiences with HD (caregiving) and their perceptions of QoL. Additionally, participants will be asked to voice their hopes and dreams for the future regarding QoL. Interviews will take ∼1.5 h. As opposed to the face-to-face sessions often seen in UCD, the interviews and focus groups will be mainly conducted through

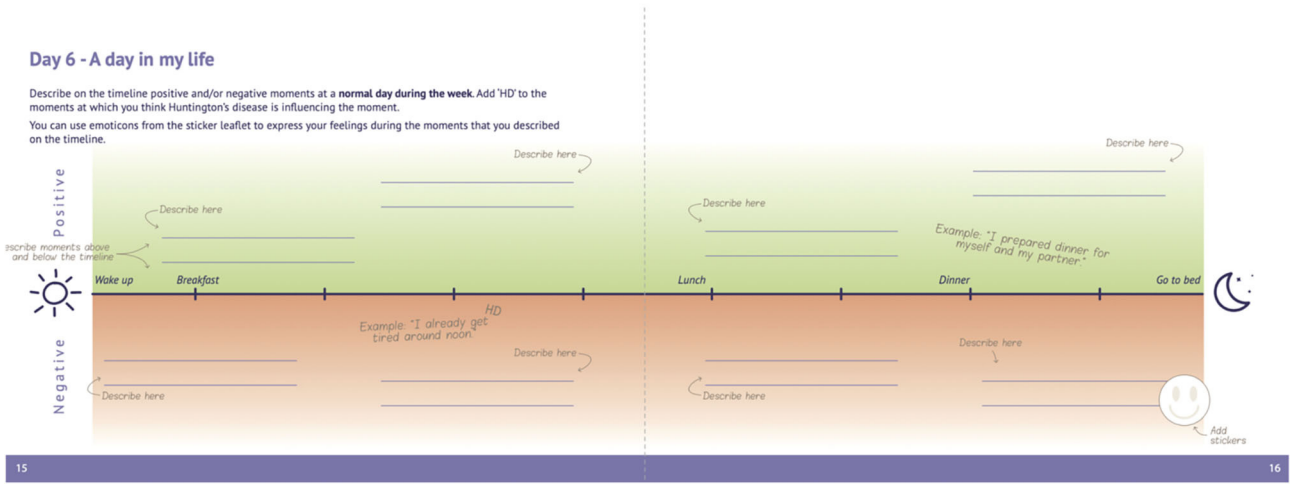

FIGURE 1 | Image of assignment in sensitizing booklet for manifest HDGECs.

online videoconferencing due to the restrictions raised by the current COVID-19 pandemic. In the case of connectivity issues, participants will be interviewed by telephone. HCPs will be asked to talk about their daily work experiences with HD during focus group sessions of ∼2 h (including breaks). Generative techniques such as patient journey mapping (58) will be applied to gain in-depth insights into the experiences of HCPs regarding HD treatment and challenges and opportunities in providing HD care. Focus group sessions will consist of a maximum of six HCPs per session and will be preferably conducted online. The groups will consist of HCPs with varying expertise in the respective countries.

HD experts from the participating research sites will provide additional information on available HD care services and the current use of eHealth technologies in HD care in their respective country to complement the information given by participants.

Phase 2: Concept Development

Based on the data gathered in phase 1 from all participating countries, we will develop concepts (through descriptions and visualizations) of the eHealth platform together with the same Dutch participants that participated in the first phase via sensitizing assignments and co-creation sessions. The sensitizing assignments will follow the same procedures as described previously. The focus in this phase will be on eHealth opportunities and possibilities (e.g., an app providing tailored practical information or a website facilitating a buddy system), yet the exact content depends on the output gathered during phase 1. The assignments will be co-developed with the HCP advisory board/FPEP and will be pilot tested with HDGECs.

During the co-creation sessions with each end-user group, problems and opportunities for eHealth, as well as solutions to address these, will be identified for all groups. Generative techniques (e.g., making a collage, journey mapping, and/or mind mapping) will be used to gather information on needs, motivations, and wishes that might not be easily expressed in words. Participants will work with tailor-made toolkits (54) consisting of, for example, paper templates, physical objects, and stickers with words and images that participants can use to reflect on their experiences with HD, generate ideas for solutions, and share them with each other (see **Figure 2** for an example of a toolkit used during a research presentation at a Huntington café). The toolkit materials will be developed and pilot tested to match the participants' cognitive and motor skills. For example, too much material on a table could cognitively overload participants who have problems with executive functioning. The co-creation sessions will generally consist of six participants and may take ∼3 h (including breaks). The sessions are intended to be performed physically, yet could also be performed online depending on the COVID-measures at the time.

The outcomes will be further developed by the research team into several detailed concepts of the eHealth platform, such as a regular monitoring service or notifications on the mobile phone. These concepts will be evaluated by the same participants during individual concept evaluation sessions of ∼1 h either at the respective site or online. Low fidelity mock-ups representing concept features will be used to evaluate the user interaction in practice. For example, the use of a mobile application will be mimicked by a paper representation of the interface in which interface elements are manually altered. The concepts will be evaluated on desirability, user-experience, and expected effect on QoL via questions and short interviews. Participants will be asked to state their preferences regarding the concepts and evaluate the concepts' fit into their daily lives. A researcher will observe the use and interaction with the concept and take notes of the interaction. The evaluation will result in a redesign of the concept and design recommendations. During this process, the international project team and the FPEP will be actively involved to evaluate concepts on their fit in the different cultures and health systems. This phase can be considered as an iterative process of designing, evaluating, selecting and adjusting concepts (59), which ends with definitive design choices for

FIGURE 2 | Example of a tailor-made toolkit.

prototypes of the eHealth platform (e.g., a definitive decision on functionalities and scenarios how the platform is envisioned to be used).

Phase 3: Prototype Testing

High-fidelity prototypes (i.e., digital representations of a product with close resemblance to the final design), as developed by the research team, will be reviewed by the same end-users that participated in the previous phase to assess usability and user-experience. The procedures for prototype testing are similar to those described above for concept evaluation. The participants' responses will be used to remove all major usability issues, such as an unclear navigation structure, and refine the user experience (e.g., a friendly or professional look and feel) in an iterative process. The same participants may be invited to perform a second round of evaluations on the improved prototype. Each individual prototype evaluation session will be held either at the respective site or online, and will take 1 h (with a minimum of 2 weeks in between, if applicable).

As soon as the major usability issues of a prototype are solved and the participants approve its usefulness, a pre-final prototype will be translated into the respective language. Newly recruited participants in each country will then evaluate the prototype during individual "think-aloud" sessions. Each session will take ∼90 min and will be preferably held at home (HDGECs/partners) or at work (HCPs). End-users will be asked to use and explore the

prototype, reflect on their experience, and express their thoughts (e.g., "What's this button for?" or "Strange picture") in the presence of a researcher. We will explore perceived usefulness, perceived ease of use, and intention to use. The findings from testing the pre-final prototype will result in a design proposal, which will then be further developed into a fully functional eHealth platform that can be tested in an RCT study.

Additional Measures

To describe the population under study and to provide additional context to the insights gained, we will collect sociodemographic information (e.g., gender, age, work situation) from all participant groups via self-report questionnaires provided with the sensitizing assignments. In addition, care-related information will be collected from partners (e.g., years of taking care of HD affected partner, care tasks) and HCPs (e.g., profession, years of working with HD).

For HDGECs we aim to also collect sociodemographic, clinical, neuropsychiatric, and cognitive data from their last or upcoming Enroll-HD visit. More particularly, we will collect, amongst others, CAG repeat length, clinical motor features of HD [based on the Unified Huntington's Disease Rating Scale (UHDRS) Total Motor Score], years of HD diagnosis (as reported by rater), independence and functioning in daily living (UHDRS Total Functional Capacity), functional status (UHDRS Independence Scale), current medication use, behavioral problems (Problem Behaviors Assessment), symptoms of anxiety and depression (Hospital Anxiety and Depression Scale), presence of suicidal ideation/behavior (Columbia Suicide Severity Rating Scale), health-related quality of life (Short Form Health Survey 12), cognitive state (comprehensive neuropsychological battery consisting of, amongst others, Symbol Digit Modalities Test, categorical verbal fluency and the Stroop Test). This additional information will provide a better understanding of specific disease characteristics and symptoms for mapping the desires and needs across different disease stages. Detailed information on the Enroll-HD measures and (informed consent) procedures are described elsewhere (51).

Data Analysis

The collected sociodemographic and clinical data will be used to describe the population under study and to provide additional context to the insights gained in each phase. A brief description of the planned data analysis corresponding with the specific procedures per phase is provided below.

Phase 1: Exploration

Qualitative data, consisting of transcripts of interviews/focus groups, field notes and other materials (e.g., filled out sensitizing assignments) will be analyzed and interpreted using thematic and on the wall analysis (54). During on the wall analysis, the office wall will be used as a large spreadsheet to label and categorize all data into clusters of themes and insights. In addition to thematic analysis, this allows the researchers to absorb the richness of the data in an unconstrained manner, which is beneficial for exploring the opportunities of eHealth through a non-linear thinking process (60). To make sure that all basic elements of QoL are covered in our findings, we use the six dimensions of positive health (61) as a benchmark: bodily functions, mental functions and perceptions, spiritual dimension, quality of life, social and societal participation, and daily functioning.

Findings from these analyses on the needs, desires, and experiences of end-users regarding QoL and HD care from all countries will be visualized in a patient journey map by the research team (58). This is a detailed schematic representation of phases and events in relation to HD and the people involved. This will be presented to the HCP advisory board, the FPEP and the international project team to align with (clinical) expert and end-user perspectives.

Phase 2: Concept Development

The HD patient journey and eHealth ideas resulting from all countries during phase 1 will be used to identify possible problem areas and points of innovation that may improve the end-user's QoL. Depending on the findings of phase 1, this may for example be to support care provision already before the onset of symptoms. Through generative sessions by the research team and the previously described co-creation sessions, ideas will be generated to address the identified problem areas and points of innovation. The resulting ideas will be clustered into a list of eHealth opportunities and strategies. Subsequently, eHealth concepts will be developed together with end-users in the co-creation sessions. Based on the qualitative data of the co-creation sessions, including transcripts, field notes and other study materials (e.g., output of sessions), low fidelity mock-ups representing concept features will be developed and evaluated. Qualitative data arising from the concept evaluation sessions will be reviewed and clustered in themes by the research team to define the design requirements for an HD eHealth platform prototype. The international project team and the FPEP will be closely involved to provide feedback and evaluate concepts on their fit in the different cultures and languages.

Phase 3: Prototype Testing

The transcripts and field notes resulting from the prototype testing sessions will be reviewed and clustered in themes by the research team to remove major usability issues and refine the user experience. Qualitative data of the "think-aloud" sessions will be clustered on problem severity in order to provide a comprehensive overview of the strengths and weaknesses of the HD eHealth platform prototype. This will be used to identify critical problems to be addressed in the development of the final prototype.

Data from all countries will additionally be analyzed to evaluate the suitability of the HD eHealth platform within different healthcare systems and acceptability within different cultural contexts. Any additional information or necessary changes resulting from this analysis will be incorporated.

Data Handling and Storage

Data will be handled confidentially. All study data will be processed, stored and disposed of in accordance with the General Data Protection Regulation (62) and all applicable legal and regulatory requirements at the respective sites. Study sessions will

be audio recorded with permission of the participants. Audio recordings will be stored on a secure disk at the respective site and will be deleted as soon as the design process is finished. Each study session will be transcribed using intelligent verbatim transcription. Non-English transcripts and study materials will be translated to English by researchers at the respective sites.

Data collection will be performed within a secured electronic case report form (eCRF). To allow secure data management and transmission between countries, the eCRF will be implemented in a Data Management System accessible at the respective sites in each country. The database will only be accessible for authorized personnel via a unique login and user ID. All participant data will be pseudonymized and identifiable data (e.g., name, e-mail, address) will be removed prior to uploading. All source documents will be stored in a secure closet for a certain period of time depending on the legal and regulatory requirements at each site.

Benefits and Risks Assessment

No risks or ethical concerns are anticipated. (Serious) adverse events are not expected due to the non-invasive character of the study. Participants will reflect on their own needs, desires and expectations regarding the disease and eHealth features during this study. This might potentially cause distress as it may be of sensitive nature for some participants given the vulnerability of this group. The researchers will be experienced and will offer the participant the opportunity to talk to an HCP in case the participant will become distressed. At the same time, these potentially unfavorable effects will be minimized by pilot testing all materials and study sessions, by mainly focusing on personal benefits and accomplishments in their management of HD and by engaging them in the development of the eHealth platform.

DISCUSSION

As a result of the neurodegenerative nature of HD, the disease causes a progressive decline in functioning and significantly influences the QoL of both HDGECs and their partners (3, 8–10, 13). Despite the emergence of HD expertise centers across Europe (2, 18, 19), we continue to face some important barriers to HD care provision, including additional costs, geographic distance of centers and availability/accessibility of these services in general (2, 13, 18). As the disease progressively advances over time, challenges to seeking or accessing care might arise (e.g., physical limitations, increased burden, cognitive/neuropsychiatric impairments), leaving those with the greatest care need behind (20). eHealth provides promising opportunities to overcome these barriers by improving the accessibility of care. In the present study, we initiated an innovative UCD study to capture the needs and wishes of HDGECs, partners and HCPs in order to develop an eHealth platform targeting QoL. The eHealth platform will be co-developed with these end-users by actively involving them throughout each stage of the design process, thereby tailoring remote HD service provision to the unique requirements of HDGECs, partners and HCPs. Given the rare nature of HD, we aim for an innovative European platform which allows for remote treatment options, information exchange and connection of experts to local clinicians beyond regional and national borders.

Some challenges might arise during the design process, including differences in healthcare systems, HD care provision and cultural context in all countries involved in this study. We will address these differences by actively involving the international project team, the FPEP, and end-users from each participating country in all design decisions. Furthermore, differences in clinical presentations and needs at different stages of the disease might pose additional challenges in developing a European platform that is both applicable and generalizable to all participants. By including HDGECs and partners across different disease stages, as well as HCPs with expertise in HD, we will be able to gather an overall understanding of the needs and desires experienced by these groups. The flexibility of UCD allows us to address a variety in needs in different ways, for instance, by 1. designing universally, 2. designing more modularly so that specific features can be added when needed, or 3. designing for specific target groups within the study population. As the HD community is very motivated and willing to participate in research, we do not expect challenges with accrual of sufficient participants in each country. Lastly, online study sessions as opposed to face-to-face sessions might pose some challenges, including connection issues, difficulties in capturing non-verbal communication, or perceived (emotional) distance between participant and researcher. We pilot-tested the sensitizing assignments and online interviews with a premanifest and manifest HDGECs (and spouse) and both agreed that online interviews were convenient and saved travel time. None had difficulties with setting up the connection, yet technical issues should be considered and an alternative way to conduct the interview (such as calling by phone) should be present prior to starting the interviews. At the same time, conducting these sessions remotely already provides a great opportunity for participants to experience online services, which greatly fits with the nature of what we are designing. In addition, this could be beneficial later on when using telehealth services, especially in the light of the shift toward a more blended care approach due to the ongoing COVID-19 pandemic (63).

Some unique aspects of this study are worth mentioning as well. Although eHealth seems promising in other neurological and neurodegenerative diseases (e.g., dementia, Parkinson's disease, multiple sclerosis) (23–30), the studies examining the benefits of eHealth in HD are limited (31–34) and often hampered by methodological challenges. In particular, these studies failed to use telehealth systems specifically designed to fit the unique perspectives and needs of HDGECs and their families, which can ultimately affect uptake later on (22, 37, 39). Actively involving end-users and addressing their needs when designing eHealth applications can be considered crucial in a disease as complex and rare as HD. In UCD, the end-user's needs are key in the choice and design of features of an application, which is important given the devastating challenges these people face and the variety in needs they might experience. Another unique aspect of this study is the inclusion of a partner group. HD does not only affect the individual but also the people in their environment. Partners of HDGECs have their own experiences and needs with regard to their QoL that should not be

overlooked. Moreover, as HD already has a tremendous impact on the QoL and needs/wishes of those affected in an early stage (e.g., tested gene positive, no symptoms) (3, 9, 11), we believe it is paramount to include the perspectives and needs of both HDGECs and their partners across different disease stages in this innovate UCD approach. By also actively involving HCPs with expertise in HD, some additional challenges that might arise in engaging HDGECs in eHealth applications can be considered in advance, such as progression in symptoms that impact needs and wishes experienced, apathy, anosognosia, denial (18), or motor impairments. Including HCPs also ensures that relevant clinical expertise will be integrated, and, at the same time, stimulates the future dissemination of knowledge and connection of experts. The eHealth platform will therefore be tailored to the unique requirements of HDGECs, partners and HCPs. We expect that this will greatly benefit future uptake, as functionalities that are desired from a user perspective will be included, and user experience and usability of the platform will be tested (37, 38, 40–42).

To conclude, an innovative European eHealth platform for HDGECs and partners will be developed based on their needs, wishes and desires, following a UCD approach. This approach allows for a personalized, tailored care platform suitable to all languages and different healthcare systems involved. After development of the platform, the eHealth intervention will be evaluated on effectiveness, feasibility and user experience in an RCT (this is not part of the UCD protocol as described in this article). We expect that an eHealth platform will enhance current HD supportive care services across Europe by making high-quality care accessible outside specialized centers (requiring individuals to travel) in the participants' homes, thereby circumventing still existing barriers in HD care provision. We intend to implement the platform, provided that the evaluation shows positive results, to ensure free availability for patients and their partners after the study. As HD is a very complex and rare disease, future studies in other rare diseases might also benefit from the adaptations to, and the results of, the participatory UCD approach described here when designing and developing eHealth applications to enhance their supportive care services worldwide.

ETHICS STATEMENT

The study was cleared for Ethics by the medical research Ethics committee of Leiden Den Haag Delft in the Netherlands (file number: N20.013). For the other research sites, Ethical approval was obtained by the local Ethics committees in the respective countries (i.e., Germany, Italy, Czech Republic, and Ireland). This study will be conducted in accordance with the principles of the Declaration of Helsinki (64) and the General Data Protection Regulation (62). Written informed consent will be obtained from all participants prior to any study-related activities.

AUTHOR CONTRIBUTIONS

EM and NC were involved in initiating and conceptualizing the project together with the HEALTHE-RND consortium, as well as funding acquisition. EM, NV, A-WH, and PL drafted the protocol. EM, NV, A-WH, PL, ED, SB, and NC were major contributors in drafting and finalizing the study protocol. PL drafted the manuscript. EM, NV, A-WH, ED, SB, NC, and WF contributed to the content and revised sections of the manuscript. All authors contributed to the article and approved the submitted version.

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Positional Manoeuvres for BPPV: Theoretical Approach to Remote Training for Non-specialists

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INTRODUCTION

The COVID 19 pandemic resulted in the extraordinary transition of many aspects of healthcare to "telemedicine" based platforms (1). While this has been a long-recognised possibility in a variety of medical specialties including stroke care (2), it was the rapidity of this transition which has been particularly striking. A close, arguably less discussed parallel to the delivery of clinical care using remote platforms, is the training of healthcare staff utilising similar technologies. Digital transformation of information and knowledge is the most recent paradigm shift (3) in our society, increasingly embraced by healthcare and academic institutions. Here we consider the possibility of leveraging such technologies to address a common, treatable clinical presentation.

Benign paroxysmal positional vertigo (BPPV) is the commonest cause of dizziness among the general population. Its incidence is conservatively estimated at 64 per 100 000 population per year (4) and is more common among the elderly population (its prevalence approaching 9% in those >65 years of age) (5). Diagnosing BPPV is important because the symptoms can be disabling and yet the disorder is easily treated. In most instances, it is thought to be caused by calcium carbonate crystals (from the otolith organs) that settle within the endolymphatic fluid of one or more semicircular canals, where they do not belong. A history of recurrent brief episodes of spinning vertigo triggered by head movement suggests BPPV, but a definitive diagnosis lies on a positional manoeuvre which will elicit positional nystagmus in patients with the disorder. **Box 1** highlights the main indications for a positional manoeuvre.

Given that BPPV may affect any one of the six semicircular canals in the head (three in each ear), one practical approach is to perform a Dix–Hallpike manoeuvre for right and left posterior semicircular canals as these are the most commonly involved (up to 95% of all BPPV cases (6). A manoeuvre such as the Dix-Hallpike should arguably be performed on every patient presenting with dizziness or imbalance because BPPV is common, carries an excellent treatment success rate, and dizzy symptoms are difficult for patients to describe (making history alone insufficient to make a confident diagnosis). Despite being an established procedure for the diagnosis and management of BPPV, positional manoeuvre are still substantially under-performed, mostly where it matters most: general practice and emergency settings, as this is where many patients with BPPV present (7). As such, there is an unmet need to improve training in positional manoeuvres across emergency, community, and primary care settings.

Assessment of the dizzy patient requires a comprehensive understanding of theory, examination and obtaining an appropriate patient history to exclude other causes of positional vertigo, nystagmus and more sinister pathologies. This degree of comprehensive assessment may be beyond the remit of non-specialists without more intensive training. Here, we focus specifically on

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BOX 1 | Indications for positional testing.

- Any patient with brief episodic vertigo, especially positional vertigo, without spontaneous nystagmus.
- Patients with otherwise unexplained unsteadiness, particularly in the elderly (where there may be a dissociation between vestibular activation and vestibular perception).
- Individuals with attacks of non-positional vertigo are unlikely to have BPPV, but a positional manoeuvre can be worthwhile. If the positional manoeuvre elicits a typical BPPV-like nystagmus the patient should undergo repositioning, but if normal the patient should be referred onwards.

positional manoeuvres for BPPV and explore aspects of a training program which may be amenable to the use of technologies or remote education. We argue that training therapists, not just physicians, is an important goal in ensuring BPPV is identified more promptly across emergency and primary care settings. In many services therapists already play a role in the assessment and treatment of BPPV, with development and access to telemedicine one possible avenue to increase the proportion of therapists who are competent and able to perform the associated manoeuvres. Communicating education through web-based technologies is commonplace–most notably, the use of video sharing platforms for interested individuals to self-direct their learning. While such platforms may contain excellent information, they potentially contain similar volumes of inaccurate and misleading content. We suggest the acceptance of web-based learning as convention provides the opportunity to develop comparative resources, scrutinised for rigour much the same way that a peer review process provides a degree of probity to the reader.

Constraints imposed during the COVID-19 pandemic saw clinical services pivot to digital technologies for a number of aspects of patient care. Here we consider if this accelerated implementation of telemedicine could meaningfully extend to training for BPPV, addressing a recognised shortfall of suitably trained healthcare staff. We describe some of the pitfalls to such telemedicine approaches, but also highlight practical factors that will increase the chances of a successful training programme and how existing technology may support this. We focus on the components which should comprise the training package for key positional manoeuvres for the diagnosis and treatment of common types of BPPV, namely Dix-Hallpike for the diagnosis of posterior semi-circular canal BPPV, and the Epley treatment manoeuvre.

COMPONENTS OF TRAINING

Components of a training program for practitioners learning assessment and treatment manoeuvres should involve both theory and practical components. **Box 2** outlines what a typical training program may include. The specific components should follow recommendations from the Barany Society (8), the British Society of Audiology procedure guidelines (9), and expert opinion regarding educational requirements (10).

BOX 2 | key components of a training program.

BPPV Training:

- Theory
- Manoeuvres training
  - Operational details
    - Room set-up
    - Subject and examiner positions
  - Supervised practice
  - Identifying the correct ear
  - Pearls and Pitfalls
- Eye movement detection
  - Nystagmus types
  - Pattern of onset
  - Video bank

Clinical observations

The practical training poses perhaps the most overt challenge given the relative paucity of specialists with training expertise, and the need to cover a wide geographical distribution for sufficient uptake to make a tangible clinical difference at a population level. Remote learning in fact may offer a practical solution by pooling the scant resource of expert educators from almost any geographical location to provide training to a widely distributed audience of learners.

Dix-Hallpike and Epley for Posterior Canal BPPV

The Dix-Hallpike manoeuvre is a simple bedside examination for the diagnosis of BPPV and can be performed with the patient placed longitudinally on the couch (**Figures 1A–C**). If BPPV is diagnosed on the Dix-Hallpike this lends itself to an Epley treatment manoeuvre (**Figures 1D–H**). If the history strongly suggests a symptomatic side, it may be best to test the non-symptomatic side first (and then do the manoeuvre on the other side) as it prepares the patient for the manoeuvre without inducing vertigo. The Epley manoeuvre is one standard treatment approach for posterior canal BPPV and involves 5 steps through which the patient's head (and body) is rotated on the couch. It requires space around the couch, but can be performed at a gentle pace, using gravity to guide movement of the offending inner ear crystals through the semicircular canal. These manoeuvres could be taught through remote teaching approaches, using video material and voice-over to guide the learner through the manoeuvre and identify common areas of difficulty or concern that learners may report. Such material could be complemented with virtual or online resources, such as a question-and-answer forum and guidance pertaining to pearls and common pitfalls for the novice non-specialist (**Box 3**).

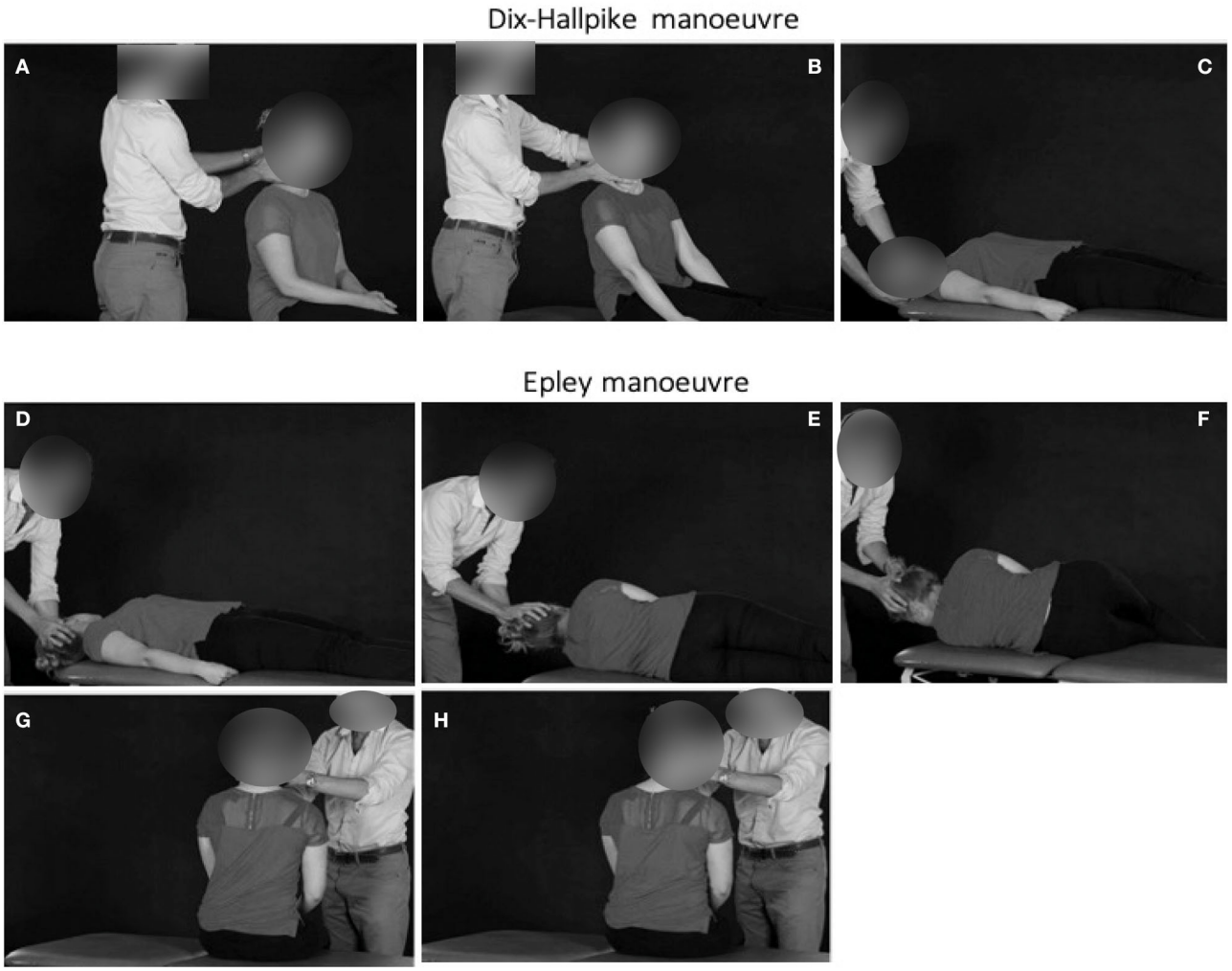

FIGURE 1 | The first manoeuvre is the Dix–Hallpike manoeuvre exploring the right ear **(A–C)**. The patient begins seated in the couch, with the feet longitudinally. The head is then turned towards the ear being explored (right ear in this case). The patient is then lowered backwards such that the head is hyperextended by approximately 30°, and overhangs the end of the couch. In the presence of BPPV, there is upbeat and torsional nystagmus beating toward the ground with vertigo, usually lasting only 5–10 s. It may be necessary to open the eyes lightly using your thumb and index fingers to see the nystagmus more clearly. Epley manoeuvre for treating right ear posterior canal BPPV **(D–H)**. After 30 s, the patient's head is rotated toward the other side [leftwards here, **(D)**], and held in this position for a further 30 s. During this time, the patient is asked to rotate the body so that he/she is lying on their left shoulder **(E)**. It is important to hold onto the head while the patient is instructed to turn, so that it does not change position. The patient's head is rotated by a further 90° to the left, to face the ground **(F)**, and held for 30 s. The patient is now sat up, with the head still looking over the right shoulder **(G)**, for 30 s. Finally, the patient's head is brought toward the midline, and the neck flexed, chin down through 45° for a final 30 s **(H)**. The procedure is reversed for left posterior canal-BPPV. *Adapted from* (11).

TRAINING DELIVERY METHODS

Remote training can take many forms. In this context we are describing the use of pre-prepared content in the form of videos and lectures and the use of online seminars that allow a distributed network of interested parties to access content through web-based platforms. One critical distinction would be the need to validate such a training program, developed and updated by expert/specialist clinicians in a suitable position to adequately scrutinise the information and communicate it effectively. Using the framework outlined in **Box 2**, we propose a training program constituted of several components, the majority of which could be completed remotely.

Theory presents the most obvious and natural component of training which could be delivered remotely. Ideally, live lecture series could be delivered through video communication software by an expert to suitable trainees. Similar approaches have resulted in positive experiences and outcomes (12), with didactic interactions, recordings of the lecture and transcription presenting a notable advantage over conventional teaching approaches.

BOX 3 | Pearls and pitfalls for positional manoeuvres.

Explanation of the manoeuvre in simple terms. Do not give too much information so as not to overwhelm the patient!

If utilising a traditional Dix-Hallpike, the manoeuvre uses gravity to mobilise the crystals within the posterior SCC, therefore it is performed with gentle slow movements.

If side-lying, the movement may need to be brisker to overcome gravitational forces, as the crystals are migrate upwards and around within the canal. You may need to get some help from the back, to hold the patient's shoulders. Ensure bed is raised appropriately to avoid injury to your back.

Patients experience heterogenous responses to Dix-Hallpike. It is common to have patients report intense vertigo, while others may deny any symptoms at all, with symptom subjectivity not always correlating to the severity of eye movements observed.

For both traditional and side-lying manoeuvres, test one side first, and the other if negative. If the first side tested produces symptoms and nystagmus, then go straight to the treatment manoeuvre.

It is unusual to have bilateral BPPV, so there is no need to test the other side after a treatment. If symptoms however persist over the coming days, it is good practice to re-test, starting with the side that was not initially treated.

Fatigability of the nystagmus can occur if the Dix-Hallpike is repeated frequently within a short timeframe. If a Dix-Hallpike is performed and the result is inconclusive, a period of 15-30 min should be allowed before retesting, with a maximum of two treatments in a single day.

Warn the patient about possible sudden unsteadiness and even risk of falls after the repositioning manoeuvre, and ensure the patient is supported immediately after the manoeuvre to avoid falls.

BOX 4 | Indications for onward referral.

There are many causes of vertigo some of which can be life-threatening, such as stroke or tumour. In any instance if the non-specialist is unsure, urgent onward referral would be advised. This would extend to any patient history which includes recent head trauma or associated neurological symptoms in addition to vertigo (e.g. headache).

Vestibular migraine is another common cause of vertigo and can be correctly identified using specific diagnostic criteria. Dizzy patients who are assessed for, but do not have BPPV should be referred onward to a specialist capable of diagnosing vestibular migraine.

Dix-Hallpike test should be applied to any patient with brief episodic vertigo (and no spontaneous nystagmus). Patients that present with spontaneous (i.e. non-positional) or gaze evoked nystagmus require urgent onward referral.

Patients with a first attack of persistent vertigo and nystagmus.

In instances where nystagmus following a positional assessment manoeuvre is difficult to characterise, or the non-specialist is feels unable to correctly define the elicited nystagmus

Nystagmus difficult to characterise or define

Nystagmus atypical for posterior canal BPPV

Downbeat nystagmus

Upbeat nystagmus

Horizontal nystagmus[1]

Nystagmus spontaneously changes direction despite head being kept in the same position

[1]horizontal canal BBPV would cause horizontal nystagmus but this is a relatively rare variant with between 5-30% of all BPPV cases.

Manoeuvre training has conventionally been taught using face to face practical sessions and departures from this approach are ostensibly viewed as inferior. However, several approaches might be considered in combination. The use of high quality well produced video content, correctly narrated can provide repeatable demonstration of the correct techniques, to be revisited by the learner as required. Video sessions, with the instructor demonstrating manoeuvres in real-time using a healthy volunteer or mannequin would allow for immediate dialogue and clarification between students and instructor. Similarly, utilising supervised remote practice, where novice learners demonstrate the manoeuvres through real-time video sessions would allow for skilled experts to observe and provide feedback on technique. Another useful tool, easily adopted by remote approaches would be to provide video examples of patients during actual assessment and treatment. While such videos typically focus on interpreting eye movements (which we outline below), an equally important component is providing learning materials which developing an understanding of the heterogenous responses patients may have, particularly to testing. For instance, when patients develop intense symptomatic responses, the specialist will typically be well positioned and able to reassure patient sufficiently to complete the assessment, while having the experience to reassure them and remain unperturbed if the patient becomes nauseous or the assessment results in emesis. Similarly, many patients respond to testing by instinctively reaching to stop themselves being lowered to a plinth or may shut their eyes to alleviate dizziness. Videos which highlight such responses are likely to better prepare non-specialists and increase the likelihood of a successful manoeuvre.

Correct interpretation of eye movements and the pattern of nystagmus is crucial to successful assessment and treatment. Utilising a video bank of typical, expected responses to assessment (positive and negative) as well as common alternative observations provides a powerful resource for the developing practitioner. Such a resource could be expanded further, to include web-based assessments where students can practice correct interpretations and be tested on their performance and accuracy.

Having undertaken positional manoeuvre training there remains the important transition of taking the newly learned skills into the clinical setting. In the context of virtual training those few specialists delivering the remote training sessions could arrange further virtual sessions to discuss some of the barriers or issues encountered while performing actual patient manoeuvres.

Benefits of Remote Training

In addition to general benefits such as the reduced travel for all participants and the ability to join from almost any location, aspects of this approach yield several other benefits which we also outline below, consistent with the Health and Care Professions Council training standards recognise that learning a new clinical skill requires theory and practical teaching, with support from experts (13). However, concerns have been highlighted on the quality of some online resources (14), which remains an important factor to consider with any such program development.

Key benefits include:

- The ability for pre-recorded content to be ready for delivery as needed.
- Possibility to scale to large number of pupils with reduced expenditure and a limited workforce of experts.
- An ability to ensure quality of content, once such a program has been validated. Importantly this avoids issues with free online content which can be excellent, however undecipherable to the nascent learner from poor content.

Risk Mitigation

There exists a real concern that training may not provide the adequate competence for the practitioner to correctly complete the manoeuvre–in this instance what are primary concerns and how might they be mitigated? We consider two aspects–the first would be any associated risk to the patient, for example, the theoretical risk of arterial dissection in the neck, or perhaps displacing of crystals to adjacent semicircular canals. The second is incorrect diagnosis, both in terms of false positive and negative interpretation of results from the assessment manoeuvre. In both such instances however, this is not a problem exclusive to *remote* training, rather a consideration for all positional manoeuvre training. Moreover, theoretical risks of injury to the patient through neck "manipulation" are not evidenced in the real-life clinical setting, largely because these manoeuvres involve neck movements that lie well within physiological limits. Pillows can used for both the Dix-Hallpike and Epley manoeuvres that further mitigate this theoretical risk and such practical advice could be easily incorporated into remote learning sessions (15). Remote learning may in fact offer an opportunity to address and reduce such risks through repeated (virtual) exposure to correct techniques. Indeed, one recent study demonstrated basic surgical skills performance (which putatively holds greater risk) could be taught to medical students online with comparable levels of competency to conventional face to face teaching (16).

As with many bedside assessments and interventions undertaken by non-specialist staff, the positional manoeuvres we describe here involve a component of patient manual handling. Incidence of serious adverse events associated with performing them is exceptionally low, and any training program should include repeated practical sessions, education to provide an awareness of the risk and supervised performance when first testing patients.

Similarly, to improve clinical sensitivity and specificity, supervised performance of the novice can provide timely feedback when first testing patients and provide an environment for accelerated learning. In addition to this convention however, training resources such as those constituted in a remote program, readily accessible, could serve to further augment the accuracy of diagnosis, by presenting practice and virtual assessment scenarios for the non-specialist to revisit during skill acquisition. In any case, the constituent program we outline here focuses on training for the non-specialist with the aim of such training to enhance the assessment and identification and treatment of BPPV. We anticipate such a program would reduce the need for specialist review in many instances, however there will remain many occurrences which necessitate specialist referral. **Box 4** provides examples when onward referral may be indicated, such guidance should form a central component of any non-specialist training, and should be adapted based on the setting and staff being trained.

CONCLUSIONS

Recent evaluations during the COVID-19 pandemic of medical student experiences using digital learning and assessment platforms suggest the majority prefer conventional approaches to learning (17). However, this does not necessarily indicate these platforms are unsuccessful or could not make a large contribution to education in future. Current trends and changes to digital communication and technologies more generally, have seen an exponential increase in online resources. As a result, the leap toward telemedicine-based solutions is far more plausible than it has been previously.

As this relates to BPPV manoeuvre training, the greatest challenge is likely to be in the practical teaching to novice practitioners. There is however no specific reason such an approach is not possible and should not be tested and validated. If proven successful, the benefits extend much further than the immediate training itself. As is witnessed in other digital technologies, such a program may address one of the greatest challenges in BPPV training *per se*, the ability to standardise and scale the resource so that quality is maintained while having the capacity to reach a greater audience.

AUTHOR CONTRIBUTIONS

VT conceptualised the idea, wrote the preliminary manuscript, and approved the final version. AM conceptualised the idea, commented critically on the manuscript, and approved the final version. DK conceptualised the idea, wrote the preliminary manuscript, compiled the figure, and approved the final version. All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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Videoconferencing Software Options for Telemedicine: A Review for Movement Disorder Neurologists

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Background: The use of telemedicine has increased to address the ongoing healthcare needs of patients with movement disorders.

Objective: We aimed to describe the technical and basic security features of the most popular telemedicine videoconferencing software.

Methods: We conducted a systematic review of articles/websites about "Telemedicine," "Cybersecurity," and "Videoconferencing software." Technical capabilities and basic security features were determined for each videoconferencing software.

Results: Twenty-six videoconferencing software programs were reviewed, 13 (50.0%) were specifically designed for general healthcare, and 6/26 (23.0%) were compliant with European and US regulations. Overall technical and security information were found in 5/26 software (19.2%), including Microsoft Teams, Google Hangout, Coviu, Doxy.me, and Thera platforms.

Conclusions: Detailed information about technical capabilities and data security of videoconferencing tools is not easily and openly retrievable. Our data serves as a guide for practitioners seeking to understand what features should be examined when choosing software and what options are available.

Keywords: telemedicine, movement disorders, Parkinson's disease, videoconference, telehealth

BACKGROUND

Advances in technology have expanded telemedicine opportunities in medical practice, research, and education. After the declaration of the COVID-19 outbreak as a pandemic, the use of telemedicine has increased to address the ongoing healthcare needs of patients with chronic illnesses, for example, by the introduction of interdisciplinary telehealth services (1–3). Such services have helped reduce the number of in-person clinic visits and thereby minimize human exposures to Coronavirus. In response to the surging needs for remote care, many countries worldwide have expanded laws and regulations to permit greater adoption of telemedicine systems, have provided increased guidance on digital health technologies and cybersecurity expectations,

and have expanded reimbursement options (4, 5). Many organizations, including the American Academy of Neurology and the International Parkinson and Movement Disorder Society, have also issued telemedicine guidelines (6, 7).

As demands increased, the pandemic caused a global surge in the use of videoconferencing tools (8). Movement disorders may be considered particularly fitting for distance health/remote visits with videoconferencing, because of the critical importance of observing phenomenology, visual aspects of the exam, speed, presence, distribution, and characteristics of tremor, dyskinesias, etc. In addition, patients with movement disorders are characterized by mobility limitations, and the sparse distribution of movement disorder specialists increasing the difficulty to access (1). Even before telehealth burst into the forefront, movement disorder specialists have been gathering videos of patients for decades at major meetings and weekly video conferences within their group. However, physicians need unbiased and expert guidance in choosing a video conferencing software, including insights into the legal framework, technical capabilities, licenses, patients' access, and costs. Compliance with software data protection requirements is likely to be different worldwide. Examples in data protection regulations include the European Union General Data Protection Regulation (GDPR), which is essential for protecting personal data in Europe. In North America, physicians would look for Health Insurance Portability and Accountability Act (HIPAA) compliant software. Given the increasing offers for videoconferencing in the market, in this article, we describe the technical and basic security standard features of the most popular telemedicine videoconferencing software platforms to inform neurologists interested in developing telemedicine programs. This review is not aimed to provide international or national-based legal information for videoconferencing tools.

PROCEDURE

For the selection of recent videoconferencing software, we conducted a systematic review of articles published since January 2020 from Medical and Telemedicine Societies, PubMed, and Google using the following keywords: "Telemedicine," "Cybersecurity," and "Videoconferencing software." Only articles and websites in English with detailed information about videoconferencing software characteristics were reviewed. We excluded supplementary applications designed to increase the security to access electronic health medical records or video-based pose estimation of movements with artificial intelligence-based analysis. The following characteristics were determined for each videoconferencing software: chat capability (ability to send/receive text messages), call capability (phone calls), videoconference capability (one-to-one, group meetings), screen share capability (ability to share your screen with different documents), healthcare-based (previous use in medicine), pricing, supported operative systems and platforms, communications protection (encryption), extra security layer, security measures in group meetings (administration of pass-invitations), Security Standard Compliance, and Privacy policy.

RESULTS

Twenty-six videoconferencing software programs were identified (**Tables 1**, **2**; **Supplementary Figure 1**). Regarding the technical capabilities, 13/26 (50.0%) were designed specifically for use in healthcare. All requested information was only found in 5/26 (19.2%) applications, including frequently asked information by users such as pricing in 11/26 (42%), and security information in 11/26 (43%) with 6 out 26 (23.0%) were both compliant with HIPAA and GDPR. All detailed information and definitions are included in **Tables 1**, **2**.

DISCUSSION

This article summarizes the main technical and security aspects of commercially available videoconferencing software for healthcare use, features that a clinician should consider while choosing a videoconferencing software. Overall, the main features of current videoconferencing software are applicable to healthcare in general and they are not specific to movement disorders. Surprisingly, we collected complete data regarding capability and security in less than 20% of videoconferencing software platforms in use, suggesting that information about technical capabilities and data security is not easily and openly accessible for interested future users. In addition, complete and explicit information on whether the vendor/subcontractors have access to the data, including the video and other medical information, was also not entirely available for review.

In this review, we have not included other essential aspects for a successful videoconference visit. Firstly, the size of the room and the number of participants where the videoconference is conducted. These aspects will determine the exact type of equipment (camera, microphone, speakers, etc.) we will need to get good video and audio quality. Secondly, it is recommended to use videoconference etiquette tips, including adequate lighting in a professional environment, eliminating background noise and looking straight at the camera, dressing professionally, and avoiding multitasking[1] (9).

Given the significantly increased use of remote care delivery during the Covid-19 pandemic, neurologists are facing an opportune time to expand the access to patients with movement disorders using videoconferencing tools (3, 10). A shift to video conferencing visits must be accompanied by efforts to prepare for and protect against breaches of security and privacy. Concern over such breaches is one of the many barriers and challenges against the more widespread adoption of telemedicine (2). Cybersecurity must be appropriately addressed to continue providing the best and safest care to our patients. To date, the most common strategies to enhance the cybersecurity of videoconferences include (1) password requirements, preventing unsolicited visitors from joining the meeting; (2) careful selection

[1]Available online at: https://www.vault.com/blogs/workplace-issues/best-practices-for-video-conference-etiquette.

TABLE 1 | Widely Known applications for videoconferencing.

	General features					Specific features			Security features					
Application	**Chat**	**Calls**	**Video Calls**	**File Sharing**	**Group video-meetings**	**Screen share**	**Healthcare based**	**Pricing (free/ license)**	**Supported OS and platforms**	**Communications protection**	**Extra security layer**	**Security in group meetings**	**Security Standards Compliance**	**Privacy Policy Statement**
Facebook messenger	✓	✓	✓	✓	✓ Up to 50 users	✗	✗	Free	Windows, MacOs, iOS, Android	E2EE	2-step verification (2FA)	Invitation, Admin control (Messenger Rooms)	SOC2, GDPR	https://www.facebook.com/about/privacy
FaceTime	✓	✓	✓	✗	✓ Up to 32 users	✗	✗	Free	MacOs. iOs	E2EE	2FA, Face ID and iPhone security	✗	?	https://support.apple.com/en-us/HT209110
Google Duo	✗	✓	✓	✗	✓ Up to 12 users	✗	✗	Free	Movil based: Android, iOs, Web browser-based	E2EE	2FA, Google Account security	Invitation and user block option	HIPAA - BAA, GDPR	https://policies.google.com/privacy
Google Hangouts (aka Meet or Workspace)	✓	✓	✓	✓	✓ Up to 10 users	✓	✓	Contact Sales	Android, iOs, Web browser-based	IETF, SRTP and DTLS client-Server	2FA Advanced protection program (APP) SSO and Google's MFA	Invitation, admin control PIN	HIPAA HITRUST SOC2 GDPR	https://policies.google.com/privacy
Jitsi Meet	✓	✓	✓	✓	✓ Without limit	✓	✗	Free and License	Windows, Linux, MacOs, iOS, Android	E2EE DTLS-SRTP	✗	Password Admin control (every user is a moderator)	?	https://jitsi.org/meet-jit-si-privacy/
Line	✓	✓	✓	✓	✓ Up to 200 users	✓	✗ No (only on Geater Tokyo Area)	Free	Windows, MacOs, iOS, Android	E2EE	✗	Invitation	?	https://help.line.me/line/android/pc?lang=en
Signal	✓	✓	✓	✓	✗ Up to 8 and no limits with chat	✗	✗	Free	Windows, Linux, MacOs, iOS, Android	E2EE	Screen Lock	✗	✗	https://signal.org/legal/#privacy-policy

(Continued)

TABLE 1 | Continued

	General features					Specific features			Security features					
Application	**Chat**	**Calls**	**Video Calls**	**File Sharing**	**Group video-meetings**	**Screen share**	**Healthcare based**	**Pricing (free/ license)**	**Supported OS and platforms**	**Communications protection**	**Extra security layer**	**Security in group meetings**	**Security Standards Compliance**	**Privacy Policy Statement**
Skype for business (part of Office 365; formerly Microsoft Lync)	✓	✓	✓	✓	✓ Up to 50 users	✓	✗	License	Windows, Linux, MacOs, iOS, Android	EE2E (private conversation)	2FA	Invitation, Admin control	GDPR, HIPAA, HITRUST, HITECH, CCPA.	https://privacy.microsoft.com/es-ES/privacystatement
Telegram	✓	✓	✓	✗	✗ Up to 1000 users and no limits in chat	✗	✗	Free	Windows, Linux, MacOs, iOS, Android	E2EE (secret chat)	2FA, block code, secret chats, and active sessions	✗	GDPR	https://telegram.org/privacy
WeChat	✓	✓	✓	✓	✓ Up to 9 users and 500 in chat	✗	✗	Free and License	Windows, Web browser-based, MacOs, iOS, Android	TLS client-Server	✗	✗	EEA	https://www.wechat.com/en/privacy_policy.html
WhatsApp	✓	✓	✓	✓	✓ Up to 8 users and 256 in chat	✗	✗	Free	Windows, Web browser-based, MacOs, iOS, Android	E2EE	2FA	Invitation	GDPR, EEA	https://www.whatsapp.com/legal/updates/privacy-policy-eea/?lang=en

(Continued)

TABLE 1 | Continued

	General features					Specific features			Security features					
Application	**Chat**	**Calls**	**Video Calls**	**File Sharing**	**Group video-meetings**	**Screen share**	**Healthcare based**	**Pricing (free/ license)**	**Supported OS and platforms**	**Communications protection**	**Extra security layer**	**Security in group meetings**	**Security Standards Compliance**	**Privacy Policy Statement**
Zoom	✓	✓	?	✓	✓ Up to 100 users on the paid version	✓	✓	License	Windows, Linux, MacOs, iOS, Android	E2EE, DTLS	2FA, SSO	Invitation, Password, Admin control	HIPAA - BAA, PHIPA/PIPEDA, SOC2	https://zoom.us/en-us/privacy.html
Teams	✓	✓	✓	✓	✓ Up to 20 users and 250 in chat	✓	✓	License	Windows, Linux, MacOs, iOS, Android, Web browser-based	E2EE	2FA	Invitation, Password, Admin control	HIPAA, HITECH, SOC2, HITRUST, GDPR	https://privacy.microsoft.com/en-gb/privacystatement

✗, *Feature not available; ?, Missing feature; ✓, Information is available. This table was designed and created by the Universidad de Burgos and Hospital Universitario de Burgos. The features of the apps and their security and privacy details shown in the table are based on the available information on April 12, (2021). If an application has two versions of its product and one of them is healthcare-based, only the healthcare-based was analyzed. The features of each health-based platform were gathered for the complete version (e.g., If there are three pricing plans for an application, the features of the complete one were selected). ? in any column means that we have not found any information. HIPAA and SOC2 (and others) are additional security standards. ADFS, Active Directory Federation Services (AD FS). It is a software developed by Microsoft. Provide users with unique credentials to access all applications within the same organization. AES, Advanced Encryption Standard is a specification for the encryption of electronic data. It was established by the U.S. National Institute of Standards and Technology (NIST) in 2001. AES can use three different key lengths: 128, 192, and 256. APP, Advance Protection Program. It is a system developed by Google, protecting users from all kinds of intentional online attacks. New protections are added automatically to deal with emerging threats. BAA, Business associate agreement. BAAs are hybrid contractual and regulatory instruments, meaning they both satisfy HIPAA regulatory requirements and create liability between the parties. CCPA, California Consumer Privacy Act (CCPA). The CCPA, approved in 2018, gives consumers more control over businesses' personal information about them. The CCPA regulations also guide how to implement the law. CSF, Common Security Framework. It is a set of documented policies and controls that govern an organization's security implementation and ongoing management. COPPA, Children's Online Privacy Protection Rule. It is a privacy act that imposes specific requirements on operators of websites or online services that collect personal information from children under 13 years of age. DTLS, Datagram Transport Layer Security. It is a protocol that provides privacy in communications. This protocol secures the client/server applications to avoid unwanted eavesdropping, unauthorized access, or message modification. E2EE, End-to-end encryption. It is a communication system where only the end users can read the messages. No third party can decrypt the data that is being communicated or stored. ECDHE-RSA, The acronym RSA comes from the surnames of Ron Rivest, Adi Shamir, and Leonard Adleman, who publicly described the algorithm in 1977. RSA is a public-key cryptosystem that is widely used for secure data transmission. 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It is a Canadian law approved in 2000 to promote consumer trust in electronic commerce and protect personal information. SAML, Security Assertion Markup Language. SAML is an open standard based on the XML-based markup language; it is used to exchange authentication and authorization data between parties, particularly between an identity provider and a service provider. SaaS, Software as a Service. It is a cloud computing model in which it is possible to pay for the use of a particular software without worrying about buying or operating that software. SIP, Session Initiation Protocol. It is a protocol used for initiating, maintaining, and terminating real-time sessions that includes voice, video, and messaging applications. It is used for private voice and video calls. SHA, Secure Hash Algorithms. They are a family of cryptographic hash functions published by the National Institute of Standards and Technology (NIST). SHA is used as a checksum to verify data integrity. SCEP, Simple Certificate Enrollment Protocol. Does IETF create a protocol designed to make the request and issuing of digital certificates as simple as possible. SOC2, System and Organization Controls, there are defined three levels SOC1, SOC2, and SOC3. It is an audit that measures the effectiveness of a cloud system based on the Principles and Criteria of the American Institute of Certified Public Accountants (AICPA). SSO, Single Sign-On. An authentication scheme allows users to log in with a single ID and password to several related yet independent software systems. SRTP-RTP, Secure Real-time Transport Protocol. An extension of the Real-Time Transport Protocol adds security features, such as message authentication, confidentiality, and response protection, mainly intended for VoIP communications. TLS-SSL, Transport Layer Security and its now-deprecated predecessor, Secure Sockets Layer. They are protocols for web browsers and servers that allow the authentication, encryption, and decryption of data sent over the Internet. MFA/2FA, Multi-factor authentication (MFA) or two-factor authentication (2FA). It is a method that reinforces the security of the applications, granting access to the system only after a user presents two or more different proofs of their identity.*

TABLE 2 | Specific healthcare based applications.

	General features					Specific features				Security features				
App.	**Chat**	**Call**	**Video Calls**	**File Share**	**Group video-meeting**	**Screen share**	**Health-care based**	**Pricing (Free/ License)**	**Supported OS and platforms**	**Communications protection**	**Extra security layer**	**Security in group meetings**	**Security Standards Compliance**	**Privacy Policy Statement**
Coviu	✓	✓	✓	✓	✓ up to 6 users in-clinic license	✓	✓	License	Web browser-based	E2EE, TLS 1.2, ECDHE_RSA with P-256 and AES_128. Coviu call, data, video and audio: DTLS-SRTP	Azure SSO, ADFS SSO, Firewall and proxy settings, API	Invitation, Waiting Area, Meeting administrator management, Security groups	HIPAA	https://www.coviu.com/en-au/privacy
Doxy.me	✓	✓	✓	✓	✓ Up to 10 users	✓ from Professional edition onwards	✓	Free and License	Web browser-based	E2EE, TLS, AES 128 with SHA256	SSO	Room passcode, access control Invitation to meeting through email	HIPAA-BAA, PHIPA/PIPEDA, HITECH, GDPR	https://doxy.me/en/privacy-policy/
Thera platform	✓	✓	✓	✓	✓ Number of users not specified.	✓ from Pro edition onwards	?	License	Web browser-based	Video encryption. Website encryption 2048-bit SSL 256-bit. Data transfer encryption. Encrypted database backups. Server encrypted AES-256 algorithm	SS0 (from Pro edition onwards)	Waiting room	HIPAA-BAA	https://www.theraplatform.com/about/privacy
Poly (ZOOM based app)	✓	✓	✗	✓	✓ up to 100 users and 100 on the paid version	✓	✓	Zoom Hardware-as-a-Service program	Windows, Mac, Android, iOS	AES-256 encryption Simple Certificate Enrollment Protocol	Remote logging with support for TLS and local account. Also, login port lockout	Authenticated access to admin menus, web interface and APIs, and security profiles	GDPR, EEA, HIPPA	https://www.poly.com/us/en/legal/privacy/privacy-policy

(Continued)

TABLE 2 | Continued

	General features					Specific features			Security features					
App.	**Chat**	**Call**	**Video Calls**	**File Share**	**Group video-meeting**	**Screen share**	**Health-care based**	**Pricing (Free/ License)**	**Supported OS and platforms**	**Communications protection**	**Extra security layer**	**Security in group meetings**	**Security Standards Compliance**	**Privacy Policy Statement**
Meetrix.io (Jitsi based)	✓	✓	✓	✓	✓ up to 500 users	✓	✓	Contact Sales	Web browser-based	E2EE DTLS-SRTP	✗	Password, Admin control:every user is a moderator	HIPAA	https://www.vidyohealth.com/privacy-policy
Vidyo Health	✓	✓	✓	?	✓ Number of users not specified.	✓	✓	Contact Sales	Windows, MacOs, iOS, Android, Web browser-based	TLS, SRTP, H.235, and AES 128-bit encryption	?	?	HIPAA	https://www.vidyohealth.com/privacy-policy
V2MD by Medisprout	✓	✗	✓	✓	✓ Number of users not specified.	?	?	License	Apple iOS, Android	Secure Socket Layer technology	?	?	HIPAA	?
Cisco Jabber	✓	✓	✓	✓	✓ Up to 600 users	✓	✗	Free and License	Windows, Mac, Android, iOS	?	?	Invitation	?	https://www.cisco.com/c/en/us/about/legal/privacy-full.html
Univago	?	?	✓	✓	✓ up to 30	✓ from Professional edition onwards	✗	Contact Sales	Web browser based	SSL/TLS, DTLS, SRTP/AES, SSL/TLS	?	Unique Meeting ID, PIN codes, encryption, lock meetings	HIPAA	https://www.yorktel.com/privacy-policy/
Medweb	✓	?	✓	?	?	?	✓	Contact Sales	Windows, Android, iOS	Secure Socket Layer	?	?	HIPAA	https://www.medweb.com/medweb-software-privacy-policy
Teladoc.Health	?	?	✓	?	✓ Number of users not specified	?	✓	Contact Sales	SaaS: web, desktop, mobile devices	?	SSO user access control	?	HITRUST CSF HIPAA AdvaMed Certified	https://teladochealth.com/privacy-policy/

(Continued)

TABLE 2 | Continued

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GlobalMed (eNcounter®)	?	?	✓	?	✓ Number of users not specified	?	✓	Contact Sales	?	Secure Socket Layer	?	?	HIPAA, ISO, FICSMA, HITRUST	https://www.globalmed.com/legal/privacy-statement/
SBR Health/Vidyo partner	?	?	?	?	?	?	✓	Contact Sales	?	?	?	?	HIPAA Children Online Privacy Protection Act	https://www.sbrhealth.com/privacy

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They are protocols for web browsers and servers that allow the authentication, encryption, and decryption of data sent over the Internet. MFA/2FA, Multi-factor authentication (MFA) or two-factor authentication (2FA). It is a method that reinforces the security of the applications, granting access to the system only after a user presents two or more different proofs of their identity.*

of software with the involvement of the IT department; (3) downloading the official release with regular updates for security patches; (4) ensuring there is no storage of video or medical data by the vendor; (5) identifying and monitoring attendees, with an alert when new attendees join the videoconference; (6) setting up waiting rooms that allow the organizer to determine whether those waiting are eligible to participate; and (7) encrypting meeting recording, making the information unreadable when obtained by third parties.

Presently and in the future, telemedicine may continue to be necessary to overcome infectious or other public health disasters/pandemics, where a healthcare response can be mobilized in a short period of time (5). In response to Covid-19 pandemic, telephone calls, messaging apps, or video visits have replaced or supplemented outpatient clinics (5). New regulations for telemedicine were created, and for example, in South Korea, the illegal status was lifted to follow established patients through telemedicine (5). Governments from several countries have initiated legislation to promote and regulate telemedicine and/or amended their prior restrictive regulations, including the US[2], Europe (11), and Saudi Arabia[3].

The strength of our conclusions is tempered by some limitations, including selection bias given the lack of information on non-English-based videoconference software. There are also important aspects to users which were not included in our table, such as "How" to conduct a videoconference (with a laptop, mobile phones, tablets) and with "Whom" (with patients, caregivers, or other health professionals), which are decisive critical factors for a successful videoconference in certain populations. We also did not elaborate on the ongoing debate concerning the best indications for the use of videconference visits in movement disorders. However, most would appear to agree that videoconferencing should be reserved for follow-up visits, intermingled with in-person visits to the hospital whenever possible, but preferably not for making a diagnosis in a new patient (12, 13). Previous literature has shown a digital gap and poor eHealth literacy (14), especially in elderly, uneducated patients, limiting telemedicine's usefulness in certain groups of patients. An extra layer of support is sometimes required to facilitate and expand the use of videoconferences by patients, including caregivers' assistance, telemedicine health personnel assistants ("telepresenters"), and the use of health care facilities designed to establish videoconferences. One of the most established telemedicine programs to date is "The Ontario Telemedicine Network" (OTN) in Canada, which employs strategies to ensure that even patients with limited technological capabilities can access telemedicine care. The OTN supports all practice specialties, including movement disorders and those with deep brain stimulation (DBS)[4]. Therefore, an optimal telemedicine program with videoconferencing should balance security aspects with user-friendliness for patients and providers, cost, browser integration, operating systems, mobile platforms, and electronic health record integrations.

In conclusion, we have described the main technical and security features of the most popular videoconferencing tools used at present. Our data serves as a checklist guide for practitioners to understand what features should be examined when choosing a videoconference software and available options. However, because technology is a science characterized by a fast evolution, it is necessary to keep updating this type of information to neurologists interested in developing telemedicine programs.

AUTHOR CONTRIBUTIONS

All authors confirm that they have significantly contributed to the review of the literature, writing and review of this article.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.745917/full#supplementary-material

[2]Available online at: https://www.commonwealthfund.org/publications/issue-briefs/2021/jun/states-actions-expand-telemedicine-access-covid-19.

[3]Available online at: https://nhic.gov.sa/en/Initiatives/Documents/TheGoverningRulesOfTelehealthEnglishEstablishingRules.pdf.

[4]Available online at: https://otn.ca; Visited at May, 10th 2021.

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Remotely Monitored Home-Based Neuromodulation With Transcranial Alternating Current Stimulation (tACS) for Mal de Débarquement Syndrome

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Objective: To determine whether remotely-monitored transcranial alternating current stimulation (tACS) may be a viable and safe treatment option for Mal de Débarquement Syndrome (MdDS).

Background: Mal de Débarquement Syndrome is a neurotological disorder characterized by persistent oscillating vertigo that is triggered by entrainment to passive oscillatory motion such as occurs during water-based travel. Treatment options for MdDS are limited, variably effective, and can be undone by further travel.

Design and Methods: This was a remotely-monitored open-label optional extension phase of a double-blind randomized onsite study of tACS for medically refractory MdDS. The primary goal was to determine safety, feasibility, and blinded participant feedback. The secondary goal was to determine efficacy. Thirteen participants (all women), aged 22–67 years, experiencing a duration of illness of 11–72 months, were a subset of 24 individuals who participated in an on-site study of tACS. They had either not responded to the on-site protocol or had relapsed after travel home. Treatment accessories and a tablet controlled tACS stimulator (Pulvinar XCSITE-100) were mailed to participants. Three teaching sessions were performed via webcam followed by on-going remote monitoring of treatment logs and participants' reports through a daily on-line diary and weekly questionnaires. Treatment continued until an effective protocol was administered for 4 weeks and then tapered over 4 weeks. Participants completed a blinded feedback survey and a debriefing interview at the completion of the entire study.

Results: Treatment duration ranged from 4 to 31 weeks followed by a 4-week taper accounting for 578 verified sessions. Of the 13 total participants, seven agreed or agreed strongly in the blinded survey that tACS treatment was beneficial; 2) Twelve were comfortable utilizing tACS on their own; 3) Eleven preferred stimulation above their individual alpha frequency; 4) Side effects were generally mild and typical of tACS. In the debriefing interview completed 2–9 months after the last stimulation, five participants reported doing "great," with no to minimal symptoms, four reported doing "good," with moderate symptoms, and four reported no change compared to pre-study baseline.

Conclusion: Remotely-monitored tACS may be a safe treatment option for MdDS with the potential for lasting outcomes, increased accessibility, and reduction in travel-related treatment reversal.

Keywords: Mal de Débarquement Syndrome, oscillating vertigo, transcranial alternating current stimulation, non-invasive brain stimulation, remote-monitoring

INTRODUCTION

Mal de Débarquement Syndrome (MdDS) is a neurotological disorder that occurs after exposure to oscillating motion such as from water, air, or land travel (1, 2). The motion perception of MdDS, typically described as a "rocking," "bobbing," or "swaying," is temporarily suppressed by re-exposure to passive motion, but worsens after the motion stops (3). Persistent MdDS lasts for 1-month or longer (1, 4). Structural brain imaging and vestibular function testing do not explain the persistent oscillating vertigo of MdDS but neuroimaging with fMRI and EEG have shown functional connectivity desynchronizations that correlate with symptom improvement that can be induced with both transcranial magnetic stimulation and transcranial alternating current stimulation (5–12).

The challenging feature of MdDS is that it is induced by travel and is worsened by travel (1, 13). Worsening by travel remains a formidable challenge to treating MdDS accounting at least in part for its intractableness since transportation is a necessary part of modern life. Thus, when patients travel for treatment, they often experience recurrence of symptoms simply because of the travel back home. This is true for treatment with non-invasive brain stimulation and with readaptation of the vestibular-ocular reflex (14–18).

Travel-induced worsening of MdDS symptoms necessitated exploring treatments that could be performed at home for extended periods of time. These included remotely monitored home-based neuromodulation options. Non-invasive brain stimulation methods for MdDS have evolved from repetitive transcranial magnetic stimulation (rTMS), rTMS followed by transcranial direct current stimulation (tDCS), theta burst stimulation (TBS), and transcranial alternating current stimulation (tACS) (14–16, 19). Only tDCS and tACS can be performed by the participant on their own given the portability and relative cost of the devices used for treatment.

Home-based tDCS was tried as an adjunctive treatment after induction treatment with 1 and 10 Hz rTMS over dorsolateral prefrontal cortex (DLPFC) in MdDS. All participants had received real rTMS but were randomized to receive either real or sham maintenance tDCS with the anode over F3 and cathode over F4 (15). A total of 556 sessions were performed by 23 participants with a 100% reporting rate. There were no major issues with safety, specifically no episodes of skin burns. This pilot study indicated that home-based noninvasive brain stimulation (NIBS) appeared feasible with high participant satisfaction (15). The device used in that study, which was started in 2013, had a sham mode but did not have monitoring capabilities, however. Therefore, true compliance could not be assessed. Furthermore, though the individuals randomized to real stimulation did better than those randomized sham stimulation, there was not a clinically significant difference in response rate, necessitating further protocol development. Since reduction in fronto-occipital connectivity induced by DLPFC stimulation correlated with reductions in MdDS severity, the next goal was to determine whether connectivity reductions could be induced more directly with tACS (9, 11).

A recently completed tACS study in 24 individuals with MdDS who had a median age of 57 years (range 22–67 years) and median duration of illness of 18-months (range 6–240 months) employed an "n-of-1" design in which all participants received three experimental protocols of fronto-occipital tACS given in a randomized order (19). The protocols were alpha frequency anti-phase (desynchronizing), alpha frequency in-phase (synchronizing), and gamma frequency (40 Hz) anti-phase active sham. Given that MdDS patients have symptoms that are worsened by travel, the treatment study design had to maintain adequate controls while not explicitly allocating patients to sham treatments that were predicted to not impart any benefit and thus knowingly raise the risk of the participants having exacerbated symptoms after traveling home. The participants were thus treated with the protocol that they themselves assessed as lowering their symptoms the most, even if it were the sham condition, after receiving all protocols during a test session. The protocol that they chose was administered for 10–12 sessions over 3 days.

There were participants, however, who were not sure what the most efficacious protocol was and could have potentially chosen a suboptimal protocol in terms of efficacy. Others felt that they had improved but, sometime after they returned home, the MdDS symptoms returned. Traveling back to the study was not a practical option. Therefore, a new option was created for these participants to try the same or a different tACS protocol in a remotely-monitored program, depending on the circumstance, for a longer period of time.

In order to safely provide this therapy, we utilized the Pulvinar XCSITE-100 transcranial electrical current stimulation device in which an accompanying Android tablet controls the stimulator through a Bluetooth connection (https://www.pulvinarneuro.com). A device management tool (TeamViewer.com) allowed the research staff to wirelessly change device settings such as the stimulation frequency (Hz), intensity (mA), and duration (minutes). The investigators could also troubleshoot problems with the participant and use the connection as a safety mechanism to turn off the stimulator if misused. The participants reported side effects for each session through an online personal weblink with these reports being verified against the usage

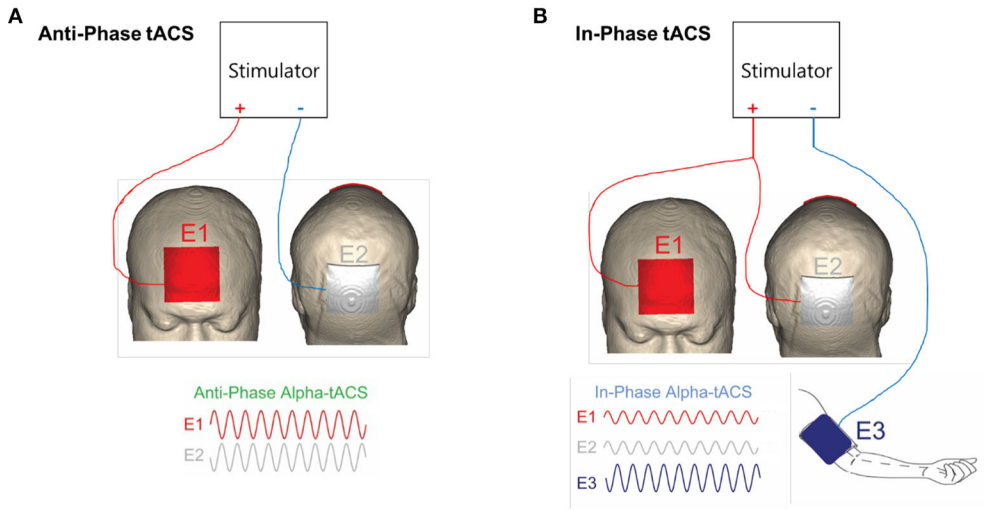

FIGURE 1 | (A) Montage for fronto-parietal anti-phase alpha frequency desynchronizing stimulation. **(B)** Montage for fronto-parietal in-phase alpha frequency synchronizing stimulation. Adapted from Ahn et al. (19).

logs reported by the device. Anti-phase vs. in-phase montages were set by whether a current splitting cable was used with a return electrode placed on the arm for the in-phase condition (**Figure 1**).

The primary aim of this study was to determine the safety, feasibility, and participant feedback of using remotely monitored tACS for MdDS. A secondary aim was to determine whether remotely-monitored user-administered tACS was effective in reducing symptoms of MdDS. If the balance of these features were favorable, NIBS could potentially be used as a primary treatment for neurotological disorders that are at least partially perpetuated by abnormal functional connectivity. It could also be used in an adjunctive manner with other forms of neurotological treatment such as vestibular therapy. The large parameter space for tACS (montage, intensity, frequency, duration), made on-site experimentation prohibitively lengthy and in some contexts (such as during a pandemic in 2021), unsafe. However, if multiple participants could be treated with concurrent protocols managed remotely, experiments could run more efficiently, provide faster feedback, and lead to faster evolution of treatments.

METHODS

All study procedures were approved by the ethics board of Western IRB (www.webirb.com) and were administered consistent with Declaration of Helsinki guidelines. Participants provided written informed consent.

Recruitment

Participants in an on-site tACS study that involved travel to the study site were given the opportunity to take part in an at-home extension phase of the study. The original group of participants were selected based on meeting inclusion criteria for MdDS, which were consistent with Bárány Society criteria (1) except that their symptoms had to have lasted at least 6-months and they had failed medically available treatments including a trial of a selective serotonin reuptake inhibitor, a benzodiazepine, and physical therapy (19). This was to ensure a favorable risk-to-benefit ratio for trying experimental therapy and to reduce risks of placebo effects.

The on-site study included 24 participants who underwent a 5-day protocol in which baseline assessments including fMRI and EEG were performed on Day 1. On Day 2, the participants received three tACS protocols in randomized order and chose the protocol that they felt most acutely decreased the perception of oscillating vertigo. The protocols were labeled, "1," "2," and "3," with the identity of the protocol blinded to both the participant and the principal investigator. The protocol that the participant decided was the most effective in reducing their vertigo intensity during a 60-min post-stimulation observation period was given over Days 3 through 5. The participants received 3–4 sessions of 20-min of tACS at 2–4 mA each day with a total of 10–12 sessions given over the 3-day period. Day 5 concluded with post-treatment fMRI and EEG (these data will be reported separately). This "n-of-1," design allowed determination of factors that were important in individual treatment effects and solved an ethical dilemma of explicitly allocating sham stimulation to participants before they traveled home.

The three protocols were as follows: 1) alpha frequency anti-phase, 2) alpha frequency in-phase, 3) gamma frequency anti-phase (active sham) (**Figure 1**). The order of administration was randomized between participants. Of the 24 participants, 13 chose anti-phase alpha frequency stimulation, 7 chose in-phase alpha frequency stimulation, and 4 chose anti-phase gamma frequency active sham stimulation.

Of the 24 participants, there were 13 who wished to try home therapy either with the same stimulation settings that they had chosen on-site, or to try a new setting, e.g., if, after unblinding, it was revealed that they had chosen the sham stimulation. They could also switch from in-phase to anti-phase or vice versa if they

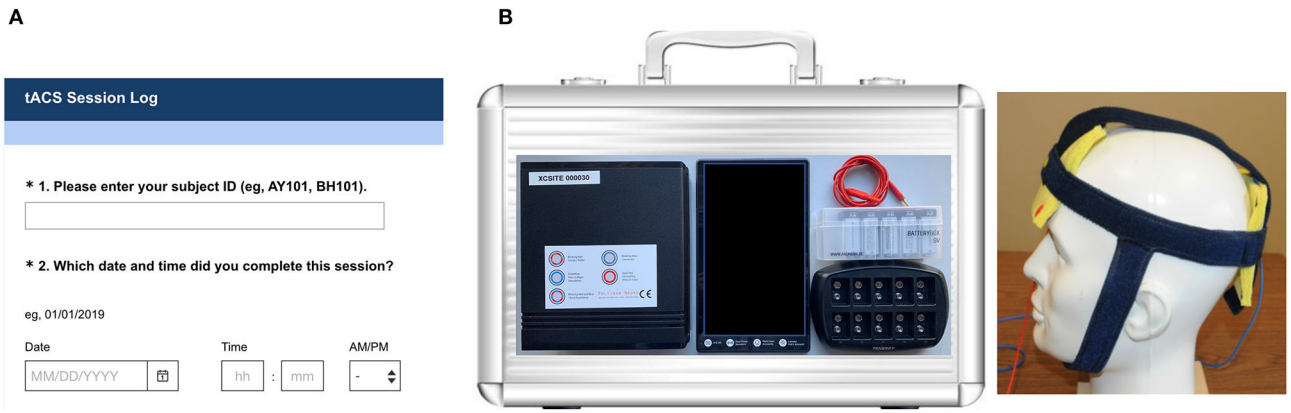

FIGURE 2 | (A) Sample screenshot of personalized weblink diary. **(B)** Device case and kit components including the Pulvinar XCSITE 100 stimulator, Android tablet, cables, electrodes, and custom fitted stimulation cap with pre-snapped electrodes.

TABLE 1 | Group level distribution percentages of side effects rated at each intensity level for a total of 578 reported stimulation sessions.

Rating	Tingling	Itching	Redness	Headache	Tiredness	Confusion	Nausea	Other
0	25.4	57.8	87.9	68.7	66.8	92.8	87.3	72.7
1	36.9	13.0	8.1	17.5	11.5	5.8	6.9	1.9
2	14.1	9.5	4.0	8.6	10.9	1.2	4.3	4.3
3	8.4	11.6	0.0	3.7	5.7	0.3	1.2	5.6
4	6.6	5.5	0.0	0.9	1.1	0.0	0.3	2.5
5	4.3	2.3	0.0	0.0	2.0	0.0	0.0	6.8
6	2.9	0.0	0.0	0.0	1.1	0.0	0.0	5.0
7	1.4	0.3	0.0	0.3	0.9	0.0	0.0	1.2
8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
10	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0

0, absent symptom; 10, intolerable symptom.

felt that the first protocol that they had tried was not effective. Finally, as we learned during the course of the tACS study, stimulating above the individual alpha frequency (IAF) was more effective than stimulating *at* the IAF. Therefore, most extension phase participants opted to try a slightly higher frequency setting than what had been used in the on-site study.

Reporting

The participants began reporting symptoms in an online diary 3 weeks before they started treatment in order to determine baseline severity levels of symptoms (**Figure 2A**). Each diary was entered through a personalized SurveyMonkey® weblink for each participant and reported every weekend. If a set of diaries was not completed by Monday morning, the participants were sent a reminder by email or by phone. Diaries included reports on the Dizziness Handicap Inventory (DHI) (20), the MdDS Balance Rating Scale (MBRS) (15, 16) (Appendix), and the Hospital Anxiety Depression Scale (HADS) (21). Additionally, after each stimulation session, the participant reported their sessions on a SurveyMonkey® link. They reported side effects from a list (**Table 1**) and rated them from 0 to 10 with 0 being absent and 10 being intolerable.

Device Kits

The participants were mailed a device kit by Week 3 (**Figure 2B**) that included the Pulvinar XCSITE 100 transcranial electrical current stimulator, an accompanying Android tablet, accessories, and the neoprene headband that had been measured for them during their on-site visit. The Android tablet was pre-programmed with the stimulation app as well as the data management tool TeamViewer for tracking. The participants purchased a single commercial brand of contact lens solution available from a major retailer to use as the conductive medium. Parameters on the app only allowed stimulation to start below a preset impedance level. The stimulation duration, frequency, current level, and impedance threshold could not be changed by the participant.

Training

Research staff used Skype® or Facetime® to walk through how to use the device and set-up the stimulation sessions with the

participants. They performed three sessions with the participant with each subsequent session having the participant perform more and more of the session themselves without prompting. The cap that had been fitted for the participants in the on-site study had electrodes snapped into the headband so that the same location on the head would be stimulated when they donned the cap. They were instructed to wet the entire sponge with saline and to avoid having any saline drip down the face or excessively wet the hair. Any extra saline not in the sponges was to be wiped away. If the hair ended up getting too wet during a set-up session, the participant was instructed to abort that session and try again when their hair was dry. If impedance was too high with just the cap, they could use an elastic head wrap to add pressure to the electrodes.

The participants were instructed to choose a quiet place for the stimulation sessions that would be free from disruptions where they could sit comfortably. They were to perform the stimulations with their eyes closed sitting in a relaxed state. Research staff stayed on-line with the participant until the session ended and were prompted to re-engage when the stimulator provided an auditory alert indicating the end of the session. The research staff then instructed the participant on how to remove the stimulator accessories and keep the components protected until the next session. Once the participants felt comfortable performing the sessions themselves, they were allowed to perform them independently without real-time staff supervision. They were aware that the sessions were being remotely monitored through the device, however, and that online reporting was being followed. Although mild side effects could be reported through the on-line diary, the participants were instructed to report any severe side effects or urgent issues through an email or a phone call to the research staff.

Stimulation Protocol

All stimulation sessions used a fronto-occipital montage at 2 mA for the anti-phase and 4 mA for the in-phase protocol. The current in the two electrodes for the in-phase protocol were split with a split cable. The return electrode was on the left arm. For the anti-phase protocol, there were two electrodes on the scalp. Stimulation sessions started with 1 session per day for 20-min for 5 days each week. When the study began, the stimulation period was limited to 5 sessions per week for 4 weeks followed by a 4-week taper (4 sessions for 1 week, 3 sessions for 1 week, 2 sessions for 1 week, 1 session for 1 week, then off). However, as we learned that the participants were quite comfortable using the device and were not developing severe side effects, we allowed subsequent participants to use the stimulator for longer periods of time. All participants were tapered for 4-weeks regardless of the total duration of stimulation. There were also periods in which the participant had to take a break because they were traveling. Therefore, there was a wide range of stimulation durations.

Participants reported performing their sessions through a personalized weblink, which included a table for reporting side effects. If the participant felt worse after a tACS session for two consecutive days, the protocol could be adjusted. Otherwise, the participant tried a protocol for at least 2 weeks before they could request a protocol change, e.g., changing the stimulation frequency (Hz). They were maintained on what they considered to be the optimum protocol for 4-weeks before being tapered off.

The number of sessions that the participant reported could be verified in the session files that were reported by the tablet which could be obtained through the device management tool. Once the stimulations were completed and the devices were returned, the participants completed an anonymous participant feedback survey administered through a separate SurveyMonkey® link. They then underwent a debriefing phone interview with the principal investigator (YHC) after all data were collected and the study had concluded. Participants were paid for the weekly diary entries but not for the stimulation sessions.

RESULTS

Thirteen participants (all women) aged 22–67 years, ranging in duration of illness from 11 to 72 months, participated in the extension phase of the tACS study. There were 23 women and 1 man who participated in the on-site study, which was open to recruitment for both women and men. Triggers for the 13 participants included seven water, five air, and one prolonged residence in a tall swaying tower. All participants had finished high school; two participants had associates degrees, seven had bachelor's degrees, and four had graduate degrees.

Side Effects

A total of 578 verified sessions were performed by 12 participants with a range of 12–214 sessions and a median of 39 sessions (**Table 1**). The time stamp on the data logs on the 13th participant could not be extracted to verify against their subjective reports and were thus not counted. Because of the wide range of stimulation session numbers, only the first 40 sessions from the two participants who had performed 90 sessions and 214 sessions were used for group level tabulations after verifying that the spread of side effects reported in the first 40 sessions was similar to the last 40 sessions for these participants. This was to avoid any one participant's experience from overweighting the group level spread of side effects reported.

The main side effects reported were tingling, headaches, itching, and tiredness mostly at a level of 3 or lower (**Table 1**). There was one report of 10/10 headache by one participant who did not report a score higher than a 2/10 for headache in any other session. Scores as high as 7 were reported by 3 participants who all reported 0's in the same category for other sessions and only on back-to-back days for tingling and phosphenes. In the "Other" category, two participants reported a metallic taste in the mouth and a third reported teeth tingling. One participant noted phosphenes and one a sense of head pulsing. One participant reported heartburn on one occasion. No side effect was severe enough to stop a stimulation session.

Participant Feedback

The participant feedback survey at the conclusion of the study indicated that most participants found three sessions of training to be sufficient with two participants indicating that more than three sessions would have been helpful (one agreed, one strongly agreed) and six participants disagreeing that more

TABLE 2 | Anonymous participant feedback survey.

Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	N/A
The online diaries were convenient	6	6	1	0	0	0
It was difficult for me to use mobile and online tools.	0	1	0	7	4	1
I felt confident setting up the stimulation sessions.	5	4	4	0	0	0
The stimulation sessions were difficult to set up.	1	0	4	6	2	0
I felt that I had enough in-person one-on-one instruction.	5	8	0	0	0	0
It would have helped to have more in-person one-on-one instruction.	0	1	2	6	4	0
I felt that I was paid enough for my time.	5	4	1	0	1	2
I would have participated without getting paid.	11	1	0	0	1	0
More instruction through Facetime/Skype would have been helpful.	1	1	5	5	1	0
More instruction through Facetime/Skype would have been burdensome.	0	1	8	4	0	0
I felt that the Facetime/Skype sessions were helpful.	8	4	1	0	0	0
Overall, I felt that transcranial electrical stimulation treatment benefited me	2	5	2	2	2	0
How comfortable would you be doing transcranial stimulation on your own without having a physician overseeing your use?	Very comfortable	Somewhat comfortable	Neutral	Somewhat uncomfortable	Very uncomfortable	
	8	5	1	1	0	
How likely are you to participate in a future brain stimulation study?	Very likely	Likely	Not sure	Unlikely	Very Unlikely	
	7	3	3	0	0	

The questions in the actual survey were presented in randomized order in both a positive and negative direction. They are presented here with like items grouped for clarity.

than three sessions would have been helpful (five disagreed, one strongly disagreed) (**Table 2**). All participants either agreed or agreed strongly that the in-person one-on-one training was sufficient. Overall, nine participants felt comfortable setting up the sessions themselves with four indicating neither agreement nor disagreement. Only one person found that the stimulation sessions were difficult to set-up. Most participants found the online diaries easy to use.

Twelve participants indicated that they were "very comfortable," or "somewhat comfortable," in managing these sessions without supervision. Two participants had responded to this question twice (thus yielding 15 responses), but only one had responded with both "somewhat comfortable," and "somewhat uncomfortable," indicating some ambiguity. Given the small number of participants, there was no demographic factor such as age or education level that predicted whether a participant would need more instruction or supervision than was given with this study design.

In the ongoing feedback with the participants, the main difficulty in stimulation set-up was in knowing how much saline to use on the electrode pads. The participants were sometimes frustrated when the stimulation sessions would not start due to high impedance measures that required restarting the sessions multiple times. This also affected when they could find time in the day to do the sessions which had to be clear of other distractions. Overall, once the participants could determine a good method for maintaining an adequate degree of sponge hydration, they reported a high level of confidence and facility in managing their own treatment.

Efficacy

In the blinded survey, seven of the 13 participants indicated that they "strongly agreed," or "agreed," that tACS was beneficial to them while four "disagreed," or "strongly disagreed" that it was beneficial and two neither agreed nor disagreed (**Table 2**). Participants completed weekly reports of the DHI, MBRS, and HADS. Because each participant experienced a different number of treatment weeks, the last 4 weeks of treatment and the 4 weeks of the tapering phase are presented in **Tables 3A–D** for the 12 participants who had verifiable treatment sessions that could be aligned with the diaries.

In the debriefing interview at the conclusion of the study, which was about 2–9 months after the final taper, five participants indicated that they were doing "great," with very minimal symptoms, four participants felt that they were doing, "good," in which some aspects of their MdDS symptoms were better but not all (e.g., no resolution of rocking but resolution of brain fog); and four participants reported having had no change from baseline. A direct comparison with the blinded survey could not be done due to the survey being anonymized, but the spread of feedback in the open interview was consistent with reports in the blinded survey. **Figure 3** shows where the participants in the extension phase study fell in the treatment spectrum of the on-site study and whether they ultimately ended up indicating their response to treatment as "Great," "Good," or "None." Efficacy appeared to correlate best with reductions in the DHI score in terms of whether the participant felt that they had had a response to the treatment (**Tables 3A–D**).

TABLE 3A | Dizziness handicap inventory (DHI).

					Last 4 weeks of stimulation change in DHI					4 weeks of taper change in DHI					
Participant	**IAF**	**Final Treatment**	**Relative IAF**	**Pre-stimulation median DHI**	**Stim 1**	**Stim 2**	**Stim 3**	**Stim 4**	**Change (%)**	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Change (%)**	**Subjective**
1	7.8	In-phase	(+) 0.8–1.1	54	−14	−22	−20	−22	−41	−30	−36	−44	−42	−78	Great
2	8.1	Anti-phase	(+) 0.4–0.7	53	−45	−39	−49	−49	−92	−41	−47	−45	−41	−77	Great
3	9.6	In-phase	(+) 0.4–0.7	13	3	1	−5	−5	−38	−3	−7	−9	−7	−54	Great
4	8.3	In-phase	(+) 0.4–0.7	36	−34	−32	−34	−32	−89	−32	−18	−18	−16	−44	Great
5	8.9	In-phase	(+) 0.8–1.1	46	−2	−2	−10	−20	−43	−10	−16	−12	N/A	−26	Good
6	8.6	Anti-phase	(+) 0.4–0.7	47	−9	−5	−7	1	2	−1	1	−17	−9	−19	None
7	10.4	In-phase	(+) 0.4–0.7	24	−6	−12	−6	−6	−25	−6	−2	−6	−2	−8	Good
8	9.3	Anti-phase	(+) 0.4–0.7	43	−1	5	3	5	12	3	5	1	−3	−7	None
9	7.9	In-phase	(+) 0.4–0.7	82	−2	4	−14	−6	−7	4	4	6	2	2	None
10	10.4	In-phase	0	64	6	6	−4	−2	−3	N/A	20	N/A	N/A	31	None
11	9.6	Anti-phase	(+) 0.4–0.7	48	14	18	18	20	42	16	26	18	16	33	Good
12	8.6	In-phase	(+) 0.4–0.7	31	−3	−3	−3	−3	−10	N/A	N/A	N/A	N/A	N/A	Great

TABLE 3B | Mal de Débarquement balance rating scale (MBRS).

					Last 4 weeks of stimulation change in MBRS					4 weeks of taper change in MBRS					
Participant	**IAF**	**Final Treatment**	**Relative IAF**	**Pre-stimulation median MBRS**	**Stim 1**	**Stim 2**	**Stim 3**	**Stim 4**	**Change (%)**	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Change (%)**	**Subjective**
1	7.8	In-phase	(+) 0.8–1.1	5	−2	−2	0	0	0	0	−2	−3	−3	−60	Great
3	9.6	In-phase	(+) 0.4–0.7	2	0	1	0	0	0	0	−1	0	−1	−50	Great
2	8.1	Anti-phase	(+) 0.4–0.7	4.5	−2.5	−1.5	−2.5	−2.5	−56	−1.5	−2.5	−1.5	−1.5	−33	Great
5	8.9	In-phase	(+) 0.8–1.1	5	−1	0	0	−2	−40	−2	0	−1	N/A	−20	Good
9	7.9	In-phase	(+) 0.4–0.7	7	−1	−1	−1	−1	−14	0	0	0	−1	−14	None
4	8.3	In-phase	(+) 0.4–0.7	5	−3	−3	−3	−3	−60	−2	0	0	0	0	Great
8	9.3	Anti-phase	(+) 0.4–0.7	6	0	0	0	0	0	0	0	0	0	0	None
6	8.6	Anti-phase	(+) 0.4–0.7	6	0	0	−1	2	33	−1	0	0	0	0	None
7	10.4	In-phase	(+) 0.4–0.7	3.5	−0.5	−0.5	−0.5	−0.5	−14	−0.5	0.5	0.5	0.5	14	Good
10	10.4	In-phase	0	6	2	0	0	0	0	N/A	1	N/A	N/A	17	None
11	9.6	Anti-phase	(+) 0.4–0.7	6	2	2	2	2	33	2	1	2	1	17	Good
12	8.6	In-phase	(+) 0.4–0.7	6	−3	−2	0	−1	−17	N/A	N/A	N/A	N/A	N/A	Great

One of the participants who reported no response subsequently developed true rotational vertigo episodes about 6 months after finishing the taper and was diagnosed with venous and arterial thoracic outlet syndrome. In retrospect, there were some symptoms of this prior to study inclusion. Thus, while no other experimental treatments were undertaken in the interim between the end of the tACS taper and when feedback was obtained, the emergence of other diagnoses, the effect of clinically available medication changes, and lifestyle modifications in the interim could not be ruled out in interpreting longer term efficacy.

DISCUSSION

This study investigated the feasibility, safety, participant satisfaction, and efficacy in remotely monitored home-based tACS for MdDS. This adds MdDS to the growing list of neurological disorders for which NIBS has been used to treat refractory symptoms (22–24). Because the very large parameter space for tACS requires refinement and tailoring, we focused on whether a home-based stimulation platform that allowed the participant to self-administer the treatment sessions may be safe as well as practical for exploring this parameter space. In order to do this, the platform needed to be controlled

TABLE 3C | Hospital anxiety depression scale-depression subscale (HADD).

					Last 4 weeks of stimulation change in HADD					4 weeks of taper change in HADD					
Participant	**IAF**	**Final Treatment**	**Relative IAF**	**Pre-stimulation median HADD**	**Stim 1**	**Stim 2**	**Stim 3**	**Stim 4**	**Change (%)**	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Change (%)**	**Subjective**
5	8.9	In-phase	(+) 0.8–1.1	6	4	−2	1	−4	−67	−1	−2	−5	N/A	−83	Good
1	7.8	In-phase	(+) 0.8–1.1	3	0	0	−1	−2	−67	−2	−2	−2	−2	−67	Great
2	8.1	Anti-phase	(+) 0.4–0.7	9.5	−6.5	−4.5	−6.5	−5.5	−58	−4.5	−8.5	−5.5	−5.5	−58	Great
9	7.9	In-phase	(+) 0.4–0.7	12	−1	−3	−7	−4	−33	−8	−4	−5	−5	−42	None
12	8.6	Anti-phase	(+) 0.4–0.7	10.5	−3.5	−2.5	−5.5	−2.5	−24	−5.5	−3.5	−5.5	−2.5	−24	None
11	9.6	Anti-phase	(+) 0.4–0.7	10.5	−7.5	−5.5	−5.5	−4.5	−43	−3.5	−5.5	−2.5	−1.5	−14	Good
4	8.3	In-phase	(+) 0.4–0.7	3.5	−3.5	−0.5	−3.5	−2.5	−71	−1.5	0.5	2.5	0.5	14	Great
8	9.3	Anti-phase	(+) 0.4–0.7	5	3	4	5	5	100	5	4	5	2	40	None
10	10.4	In-phase	0	9	4	3	−2	−2	−22	N/A	5	N/A	N/A	56	None
7	10.4	In-phase	(+) 0.4–0.7	3	2	−1	3	1	33	1	2	−1	2	67	Good
3	9.6	In-phase	(+) 0.4–0.7	1.5	−0.5	1.5	−0.5	−1.5	−100	−1.5	5.5	1.5	4.5	300	Great
6	8.6	In-phase	(+) 0.4–0.7	7	0	0	0	−1	−14	N/A	N/A	N/A	N/A	N/A	Great

TABLE 3D | Hospital anxiety depression scale-anxiety subscale (HADA).

					Last 4 weeks of stimulation change in HADA					4 weeks of taper change in HADA					
Participant	**IAF**	**Final Treatment**	**Relative IAF**	**Pre-stimulation median HADA**	**Stim 1**	**Stim 2**	**Stim 3**	**Stim 4**	**Change (%)**	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Change (%)**	**Subjective**
5	8.9	In-phase	(+) 0.8–1.1	4	−3	−4	−3	−4	−100	−3	−4	−4	N/A	−100	Good
2	8.1	Anti-phase	(+) 0.4–0.7	4	−2	−2	−3	−3	−75	−3	−2	−3	−3	−75	Great
4	8.3	In-phase	(+) 0.4–0.7	6.5	−4.5	−4.5	−4.5	−4.5	−69	−4.5	−4.5	−2.5	−3.5	−54	Great
11	9.6	Anti-phase	(+) 0.4–0.7	13.5	−7.5	−4.5	−5.5	−4.5	−33	−7.5	−5.5	−6.5	−6.5	−48	Good
6	8.6	Anti-phase	(+) 0.4–0.7	9.5	−4.5	−6.5	−7.5	−2.5	−26	−8.5	−3.5	−5.5	−4.5	−47	None
9	7.9	In-phase	(+) 0.4–0.7	11	0	1	−4	−3	−27	0	0	−3	−2	−18	None
7	10.4	In-phase	(+) 0.4–0.7	3.5	−1.5	0.5	−0.5	−0.5	−14	−1.5	−1.5	−2.5	−0.5	−14	Good
1	7.8	In-phase	(+) 0.8–1.1	1	−1	0	−1	−1	−100	−1	−1	−1	0	0	Great
10	10.4	In-phase	0	11	1	0	−2	−1	−9	N/A	1	N/A	N/A	9	None
3	9.6	In-phase	(+) 0.4–0.7	1.5	−0.5	−0.5	1.5	−0.5	−33	−1.5	−0.5	−1.5	1.5	100	Great
8	9.3	Anti-phase	(+) 0.4–0.7	5.5	3.5	2.5	4.5	3.5	64	3.5	4.5	5.5	5.5	100	None
12	8.6	In-phase	(+) 0.4–0.7	6	1	1	2	1	17	N/A	N/A	N/A	N/A	N/A	Great

*Participant IDs are anonymously labeled in **(A)** according to greatest change in DHI after the 4 weeks taper. The same IDs are preserved for **(B–D)**. IAF, Individual Alpha Frequency. Column 4 reflects the final treatment frequency used relative to the IAF.*

remotely, have safety restrictions, and be user-friendly enough to encourage adherence.

Safety

Side effects were similar to those reported in tDCS and tACS studies and generally did not last past the duration of stimulation sessions (23). This is with the caveat that the majority of human NIBS studies stay within 1–2 mA ranges of stimulation intensity, corresponding to a current density of <0.15 mA/cm2 (25). In this study, the in-phase stimulation was administered at 4 mA split into two electrodes, yielding a maximum current density of 0.02 mA. Rare persistent skin irritations have been reported as well as unmasking hypomania or mania in patients with either unipolar or bipolar disorder in other NIBS studies (26, 27). In the thousands of sessions of tDCS and tACS that have been reported to date, the overall safety profile has been excellent.

The vast majority of home-based transcranial electrical stimulation trials have used tDCS as it has been used more widely and earlier than tACS in laboratory settings. So far, stimulation side effects appear to be very similar between the two modalities, but frequency related phosphenes can be induced by alternating current both by retinal and cortical stimulation in tACS which pose additional challenges in safety and adequate blinding in controlled studies (28, 29).

Side effects in this home-based study were generally mild with the rare severe side effect being inconsistent. All stimulation

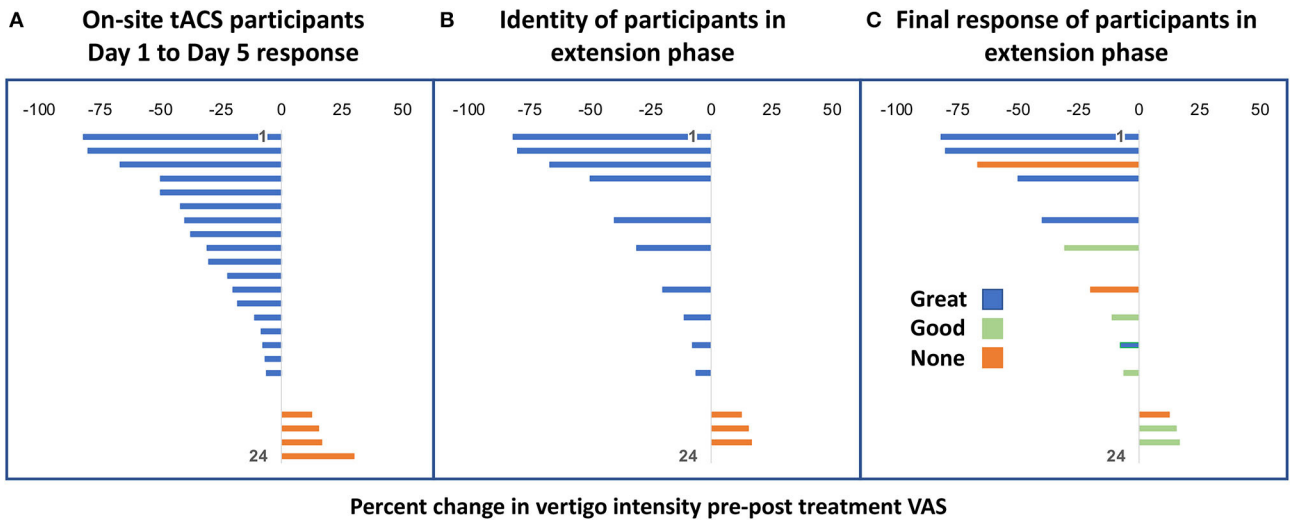

FIGURE 3 | (A) Percentage change of oscillating vertigo intensity from Day 1 to Day 5 of on-site tACS treatment of 24 participants. **(B)** Identity of the 13 participants in the extension phase from within the on-site group of 24 participants. **(C)** Final treatment response of the 13 participants as "Great," "Good," or "None" shown in relation to their original response level from their on-site participation.

sessions were completed and there were no reports of skin burns. While there were 13 individuals who completed a very high number of sessions safely, it should be noted that all participants had previously been screened to be in generally good health, had normal structural brain MRIs, had no implanted devices (e.g., pacemakers), and had tolerated in-person treatment sessions with tACS. Risks are not generalizable for individuals who do not pass similar safety screens.

Monitoring

Despite side effects being uncommon, monitoring is still warranted for potential rare events in NIBS studies (26, 27, 30, 31). The goal for home-based treatment is for research participants and eventually patients to be able to use the simulation devices independently, but safely, and to develop judgment on when to ask for assistance.

The strategy we employed of providing at least three concurrent monitored sessions of tACS and being available for questions by email and phone worked well for our particular cohort of research participants. Despite the majority of the sessions not being monitored in real time, the participants did know that the data that they were entering was being monitored. They were also assessed every couple of weeks to determine whether the protocol they were currently using was efficacious. Although this may have introduced more variability in determining efficacy, it allowed us to test the ability of the research staff to remotely access the tablet that controlled the stimulator box in order to change the protocol. The participant was always aware of when a protocol was being changed.

We used two levels of monitoring. First, the Pulvinar XCSITE-100 device creates a user log that has a timestamp. Remotely accessing the user log allowed the research staff to verify whether the participants had performed the stimulation sessions. They could also determine how many sessions the participants had triggered before they could get a successful session indicating how difficult the participants found setting up the sessions. The main reason for multiple session initiations was the impedance being too high.

Second, the participants were asked to report any side effects in an online diary for each session. This allowed the research staff to cross check participant reports with the simulator output reports. The participants also completed a more intensive questionnaire once a week. The questionnaires could be completed within 30 min with the time to completion recorded. While the intensive data collection created much more research personnel time for tracking, it also served as a reminder to the participant that they were actively in a study despite not being engaged in ongoing live interactions. This helped the study maintain a high adherence rate.

Participant Feedback

Overall, participants reported high confidence in performing the sessions and using the online tools. All participants felt that they had enough one-on-one instruction. One person felt that more online helped through the webcam would have been helpful while one participant felt that more webcam help would have been burdensome. Most participants were satisfied with the level of monitoring but one participant reported feeling that she was somewhat on her own. This highlights the difficulty in balancing the amount of supervision that participants need for confidence in self-management versus their sense that they are still sufficiently monitored. The adequacy of time was not for technical expertise in performing the sessions, of which all participants became quite competent very quickly. Rather, it was how much interaction with the research staff participants needed to feel that they were receiving adequate attention throughout

the course of their treatment. While some individuals may welcome the autonomy of self-treatment that NIBS provide, other individuals may feel that they have missed out on an important part of the therapeutic effect by not meeting with the treatment provider in person.

Feasibility

Feasibility of managing a remote treatment study required adequate staffing for monitoring reports, funding for mailing the device kits back and forth, and having the ability to troubleshoot technical issues in real time.

From a study management standpoint, the main issues the investigators faced involved keeping track of the large amount of incoming data. The participants were instructed to contact the study coordinators immediately if they had any serious or concerning side effects but less urgent issues were reported in the diaries. When participants requested a change of protocol, an assessment had to be made about the role of contributing factors such as recent travel, sleep deprivation, weather changes, work, or stress in the treatment response. Other monitoring work involved following up on incomplete questionnaires, answering participant questions, and trouble-shooting electronics issues. Managing these issues required significant personnel time.

The participants were mailed the kits and were provided with paid postage to return the kits. Over time, postage costs add up. Because this was a study, the participants were paid to complete the diaries but were not paid for individual sessions which were tailored around their individual treatment responses. A few devices had to be switched out for repairs in the middle of the sessions. All devices were returned at the end of the study. If the devices had not been returned, this would have amounted to a large monetary loss to the study. However, the data management tool allowed the device to be made unusable if not returned and was fortunately not needed for this purpose.

Efficacy

This home-based treatment program allowed the participants to try different protocols in terms of frequency of stimulation relative to their IAF with almost all participants eventually treated at a frequency above their IAF. The remote nature of the study allowed more time to tailor these treatment parameters. In the blinded survey at the conclusion of the study, seven out of 13 participants indicated benefit from the additional exposure to tACS which closely matched the five out of 13 participants who noted doing "great" and three participants who indicated doing "good," in the open interview. Considering that the participants had been medically refractory prior to participating in the study, any additional improvement in status was positive though evidence of efficacy was not as strong as a direct head-to-head comparison to a sham condition.

The participants completed the same questionnaires that have been used in all of our prior neuromodulation trials, namely the DHI, MBRS, and the HADS depression and anxiety subscales. The numbers of participants were too small to determine the main parameters that drove efficacy but four participants chose anti-phase and eight participants chose in-phase stimulation. There was no difference in mean efficacy between the anti-phase and in-phase treatments because of the very large degree of variance in responses. We had previously shown that the anti-phase condition was usually more effective than the in-phase condition in reducing synchrony as measured by the auditory steady state response (19). The in-phase condition in some participants was more effective, however. In some individuals, the slight phase delay in fronto-occipital transmission might be sufficient to render in-phase stimulation to be desychronizing. There were too few instances of each response category to determine which outcome measure had the strongest correlation with overall perception of treatment response but there was general aggregation of responses correlating with the DHI (**Table 3A**) followed by the MBRS (**Table 3B**) and less so with the HADS (**Tables 3C**,**D**). It should be noted that not all symptoms of MdDS were adequately captured by these scales. For example, one participant reported that her brain fog had resolved after the treatment despite persistence of her rocking vertigo.

Unfortunately, the study timeline was fixed so it was ended before more participants could try additional protocols. It is possible that some participants may have had a better ultimate response if given more opportunities to tailor their treatment. Correctly attributing treatment efficacy may also be difficult because of constant sources of motion in daily life and other changes such as home and job relocations, dietary and exercise changes, and medication changes for reasons other than MdDS.

Though home-based tACS has not been as prevalently tried as tDCS, new studies are emerging; treatment of MdDS with tACS is currently one of the few reported. A double-blind randomized sham-controlled trial of low intensity tACS (0.4 mA) at 140 Hz over visual cortex was used for migraine abortive treatment in 25 participants (16 real, 9 sham). Stimulation was provided with the NeuroConn, which could store stimulation sessions though not reporting in real-time. Participants had a mean age of about 30 years and had experienced a mean of 14 years of migraines. Adherence was low (25 of 40 completers) but the percentage of aborted migraines at 2-h in the treatment group (14 of 38 migraines, or 37%) was significantly higher than in the sham group (0 of 23 migraines, or 0%) (32). Despite the high efficacy, the main driver of low adherence was the difficulty in setting up the stimulation to treat acute migraines.

Additionally, a recent pilot study reported on two 79-year old patients with Alzheimer's related dementia in which focal 40 Hz stimulation was given over the left angular gyrus using the Starstim Neuroelectrics simulator. The 70 sessions performed over 14-weeks were administered by a spouse with excellent tolerability and adherence. Improvement was assessed on the non-visual Montreal Cognitive Assessment (25). Though current shunting through the cerebrospinal fluid can present a problem when electrodes are placed at a distance on the scalp, focal stimulation using a 4×1 montage with placement informed by electrical field modeling as in this study may be able to address shunting issues.

Limitations and Challenges

The study used an open label design in order to optimize study management issues. Though we did not have a sham condition

in this study, future remotely-monitored NIBS studies could allow investigators to remotely change stimulation settings in a blinded manner. A remote study would remove the ethical dilemma of requiring participants to travel to a study site and potentially receive sham stimulation in the setting of raising the risk of travel related symptom exacerbation. These studies could be done in a triple blinded manner in which the participant, the principal investigator, and the data analyst were all blind to the treatment allocation.

We note that all of our participants had participated in a more intensive on-site study and thus understood what the experience of tACS would be like. They were already adept at using on-line diaries. They had been sent their own stimulation cap which had been measured for them. In future iterations of the study, participants could be walked through how to make head circumference measurements themselves in order to snap the electrodes into the correct place.

Though most of these components were designed to be user-friendly for individuals who can casually use a computer, this may not be the case for all potential participants. Making accurate assessments of participant comfort and capability are critical to making remotely-monitored NIBS a sustainable treatment option with some individuals potentially needing the help of a second operator for set-up and maintenance.

Future Use of Non-invasive Brain Stimulation

Remotely-monitored NIBS can increase the number and type of patient who can access research studies and ultimately clinical care using these therapies. Specifically, patients who live in rural areas far away from major research centers, those with jobs with inflexible hours, families with childcare obligations, and patients with limited transportation options would be the most likely to benefit. The protocols for this MdDS study were developed through determining functional connectivity markers that correlated with symptom improvement in MdDS. These tools could be adapted to study other functional neurotological disorders to develop diagnosis or even symptom specific protocols.

Navigating safety, feasibility, and user feedback for NIBS methods may allow a future in which NIBS is prescribed just as patients are currently prescribed medications. Patients are currently entrusted to manage their own medications with incredible freedom. Education and proper respect for the limitations of what NIBS can achieve for treating neurotological disorders are needed. As with medications, patients should be advised that more is not always better, that treatment effects may not only plateau but potentially worsen with more sessions, and that protocols that are prescribed for one individual should not be used on other people.

If NIBS could be provided with device protections such as capping the total amount of current deposited in a treatment session, aborting sessions that have high impedances, and restricting the number of sessions that could be performed per month, there may be enough built-in protections to allow patients to be given autonomy in treating themselves. They may even develop a sense of self-efficacy from managing their own treatment. Just as some medications are best taken in the morning, others at night, and many require multiple doses throughout the day, this will likely be true of NIBS treatments. Since it is impractical for treatment providers to monitor every session of NIBS in real-time, stimulation devices may be configured to send usage reports, build in side effect reporting, and send urgent notifications for more serious side effects. Patients do require different intensities of supervision as well as the need for live interactions with either the research staff or care provider in order to maintain a therapeutic relationship. On-going user feedback is important in titrating an optimal amount of supervision that balances safety, autonomy, adherence, and efficacy.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because an appropriate data sharing agreement must first be agreed between institutions before they can be shared. Requests to access the datasets should be directed to ycha@umn.edu.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Western IRB. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

Y-HC designed the concept of the study, performed recruitment, and wrote the manuscript. JR performed data analysis and reviewed the manuscript. DG performed recruitment, data management, and participant management. BD performed data management, remote monitoring, and technical troubleshooting. All authors were involved in some combination of design, data collection, analysis, and manuscript preparation.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.755645/full#supplementary-material

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Remote Evaluation of Parkinson's Disease Using a Conventional Webcam and Artificial Intelligence

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Objective: This study aimed to prove the concept of a new optical video-based system to measure Parkinson's disease (PD) remotely using an accessible standard webcam.

Methods: We consecutively enrolled a cohort of 42 patients with PD and healthy subjects (HSs). The participants were recorded performing MDS-UPDRS III bradykinesia upper limb tasks with a computer webcam. The video frames were processed using the artificial intelligence algorithms tracking the movements of the hands. The video extracted features were correlated with clinical rating using the Movement Disorder Society revision of the Unified Parkinson's Disease Rating Scale and inertial measurement units (IMUs). The developed classifiers were validated on an independent dataset.

Results: We found significant differences in the motor performance of the patients with PD and HSs in all the bradykinesia upper limb motor tasks. The best performing classifiers were unilateral finger tapping and hand movement speed. The model correlated both with the IMUs for quantitative assessment of motor function and the clinical scales, hence demonstrating concurrent validity with the existing methods.

Conclusions: We present here the proof-of-concept of a novel webcam-based technology to remotely detect the parkinsonian features using artificial intelligence. This method has preliminarily achieved a very high diagnostic accuracy and could be easily expanded to other disease manifestations to support PD management.

Keywords: Parkinson's disease, kinematics, webcam, telemedicine, artificial intelligence and bio-inspired algorithms

INTRODUCTION

Bradykinesia, defined as the slowness of movement and decrement in amplitude or speed (or progressive hesitations/halts) in continuous movement, is the most relevant clinical motor feature of Parkinson's disease (PD) (1). For its evaluation, the clinicians analyze the multiple aspects of movement, such as amplitude, speed, fatigue, and arrests when executing a motor task. Typically, a clinician integrates all these features. The best example is its rating into a single severity score

of different bradykinesia tasks part of the Movement Disorders Society-sponsored revision of the Unified Parkinson's Disease Rating Scale motor subscale (MDS-UPDRS part III). This scale is the most used standard evaluation of motor function in PD (2) with a high test–retest reliability and inter-and intra-rater reliability (3, 4). However, it is an ordinal scale with only five discrete categories, and often its accuracy can be compromised due to the subjectivity of the assessment and the difficulty to detect the subtle changes in the consecutive time points.

To accurately quantify and analyze the motor performance of the patients with PD, the technology-based tools, such as the wearable sensors composed of accelerometers and gyroscopes can be used (5). These objective measurement tools can overcome the subjective and non-linear measures resulting from the clinical ratings (6). Additionally, they can be used to analyze the motor status of the patient in the home setting (7).

The optical motion capture systems based on video processing can also be used to study motor performance (8, 9). Specifically, some video-based systems are developed for the automated assessment of the upper limb movement in the patients with PD (10). These systems included cameras combined with the colored and reflective markers, bare hand tracking by the depth-sensing devices that traced the upper limb movement while performing the MDS-UPDRS part III bradykinesia tasks (11–13). These systems are traditionally used in a lab setting and have not yet been transitioned to the home environment. With the surge of telemedicine and remote consultation, there is a need for the supportive tools that permit an objective evaluation of movement remotely.

In this work, we propose a markerless video-based motion method to prove the concept that video-based objective classification of PD motor function based on bradykinesia is possible using a standard laptop webcam and an artificial intelligence algorithm. This analysis provides an ideal proof-of-concept for capturing bradykinesia of a patient with PD remotely while using an accessible, standard webcam video-camera.

METHODS

Subjects

We recruited a consecutive cohort of 22 patients with PD and 20 healthy subjects (HSs). The eligible patients (i) had a PD diagnosis in the preceding 5 years according to the UK Brain Bank Clinical Criteria (14), further supported with (ii) a PET-^{18}FDopa neuroimaging. We excluded the HSs in the presence of personal history, and first- and second-degree family history of any movement disorder (i.e., tremor or parkinsonism), and any known condition that could affect motor performance of the upper limbs. The demographic characteristics were assessed for both the groups, such as handedness (Laterality Preference Index, LPI) (15). An independent dataset containing $N = 12$ videos (six PD and six HSs) were also included as validation cohort for the test. The Ethics Committee of HM Hospitales approved the study protocol (protocol number: 18.05.1245-GHM). The participants provided the written informed consent before participating in the study.

Clinical and Quantitative Motor Assessment

The participants were always evaluated after overnight *off* medication, and clinical evaluation included a motor assessment performed by two trained specialists (MHGM and ASF) using the MDS-UPDRS Part III. To evaluate the concurrent validity of the new method with other objective tests, motor performance was also evaluated with objective measures using the inertial measurement units (IMUs) (Kinesia^{TM} One system; Great Lakes Neurotechnologies Inc., Cleveland, OH, USA) (16). We quantified the motor function while performing the MDS-UPDRS-III bradykinesia upper limb tasks (finger tapping, hand movements, and pronation and supination movements of the hand). For that, the IMU was placed on the index finger. Output data from Kinesia^{TM} is a continuous score from 0 (less) to 4 (maximum) impairment.

Video Data Collection

The participants were recorded with a computer webcam (640 $\times$ 426 pixels at 30 fps). During the examination, the participants rested their elbow on an armchair, and the camera was adjusted such that the hand and forearm were always present in the field of view. The participants were instructed to perform the MDS-UPDRS III bradykinesia upper limb tasks (finger tapping, hand movements, and pronation and supination movements of the hand) in front of the camera. Each task was performed three times with each hand separately (i.e., single-hand tasks, named unilateral motor tasks), and with both hands simultaneously (i.e., two-hand tasks, named bilateral motor tasks). For the normalization purposes, for each task the subjects were asked to stay in a certain position for a few frames. In the finger tapping and hand movements tasks, the patients were asked to do a maximum aperture and closing of the fingers or hand. In the pronation and supination movement of the hand task, the subjects were asked to extend the arm with the palm down and do the maximum supination movement. Each video sample was restricted to 12 s.

Image Analysis

The video frames were processed with a Single Shot MultiBox Detector (SSD) network trained to detect the hands in real-time using the EgoHands dataset (17). The output of the SSD is a series of bounding boxes each marked with the probability of it containing a hand. The algorithm detects each hand and processes each of the two bounding boxes separately. To refine the detection process, we introduced some post-processing rules depending on the task. For single hand tasks, we selected the highest-ranking bounding box on the side required by the task, and for the two-hand tasks, we selected the highest-ranking bounding box on each side. We also performed a temporal correction. If the probability of a certain bounding box was not higher than its probability in the previous frame, we keep the previous bounding box. This pre-process ensures a correct and efficient detection of hands due to a varied background of the videos. After the bounding boxes for the hands were computed for all the frames, these boxes were cropped and processed by a second CNN model named OpenPose (18), to detect the joints

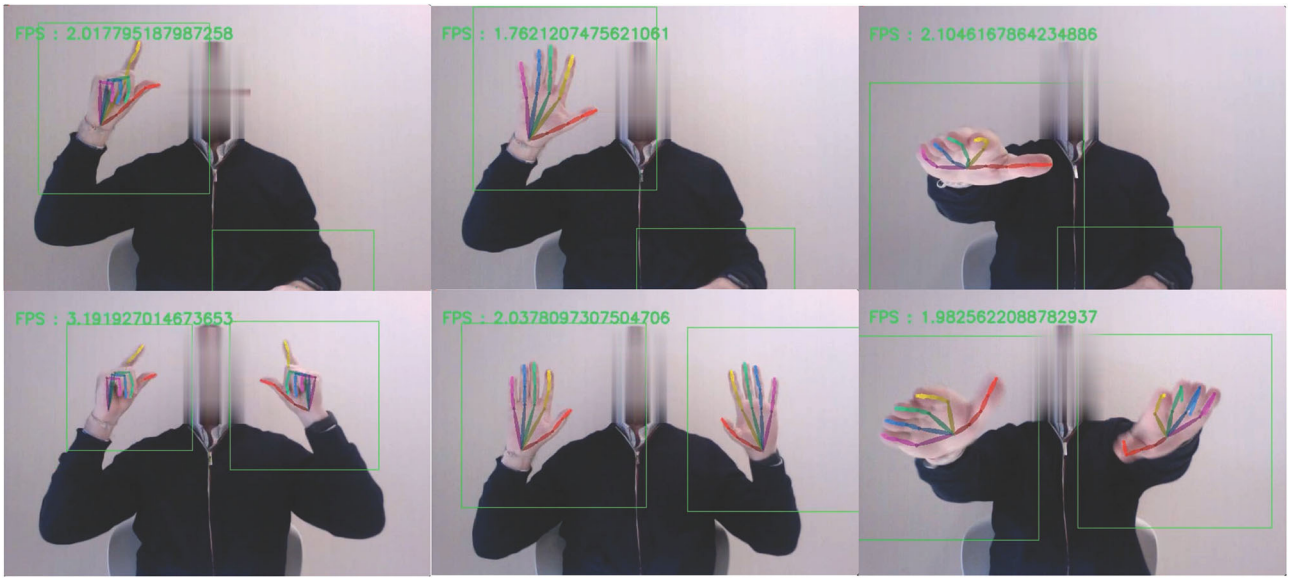

FIGURE 1 | Video-capture motion. Example of finger tapping, hand movement, and pronation supination movement of the hand while performing the single-hand **(upper)** and two-hand **(bottom)** motor tasks. The bounding box is represented in green. The color markers over the hands represent specific landmarks extracted by OpenPose.

of the hands (**Figure 1**). The specific landmarks extracted by OpenPose for each hand are shown in **Supplementary Figure 1**. From these landmarks, we select specific key-points to generate time curves to describe each task. To compensate for the camera distance and the size of the hand in the amplitude measurements, we normalized the measurements to the maximum amplitude. For finger tapping, the Euclidean distance (in pixels) between the thumb and the index finger was computed for every frame. For the hand grasp task, the Euclidean distance in pixels between the wrist and the average of the tips of all fingers, except the thumb. For the pronation-supination task, we computed the vector resulting from subtracting the key points of the pinky finger and the thumb. This vector was then transformed into the polar coordinates to obtain the degrees of the rotation for every frame, with respect to the normalization frames, as explained above.

The time signals were pre-processed with a Butterworth low pass frequency filter. To select the frequency of the filter we computed the Fourier transform of each graph to calculate their frequency components. The frequency selected to perform the low pass filter was the highest frequency of the peaks that have an amplitude at least higher than one-fourth of the amplitude of the highest frequency peak.

In addition, we applied an amplitude correction, to eliminate the peaks due to noise. For the finger tapping task, we used a normalized pixel threshold of 0.1, while for the hand grasp and pronation/supination tasks, a 0.25 threshold was applied. After filtering every signal, we extracted the upper envelopes of the filtered signals, by detecting the peaks and interpolating among them (**Figure 2**). We extracted several features from the time curves: mean amplitude and SD of the peaks, speed (number of peaks per second), and fatigue (difference between the highest and the lowest values of the upper envelope of the curve). The three features were computed for both the left-hand and the right-hand tasks.

To confirm the accuracy of the time signals generated by our pipeline, the videos were assessed by an external clinician that manually labeled every landmark of the hand in videos of the finger tapping task of nine subjects. The clinician labeled the frames from each video of both hands and the software skipped two frames after each labeled frame. The salient points were automatically extracted for the remaining frames by the algorithm. Visual inspection of the salient points aligned to the original video were used to confirm the accuracy of the algorithm output.

Classification Model Design

We designed a model to differentiate between the PD and HSs. For this, we extracted several single features that are known to be related with bradykinesia (mean amplitude, SD of the amplitude, speed, and fatigue) (19, 20) from both the hands either in the single-hand tasks and in the two-hands tasks. We trained three classifiers: Logistic Regression, Gaussian Naive-Bayes, and Random Forest. Each classifier received two values as input. These were the values of each feature for the left and right hands, respectively. We trained the classifiers using the features from each hand in the single hand tasks and using the features from each hand in the tasks performed with both hands simultaneously. A 4-fold cross-validation per classifier was applied and the receiver operating characteristic (ROC) curve per fold of the classifier was produced. Subsequently, an average ROC curve was calculated

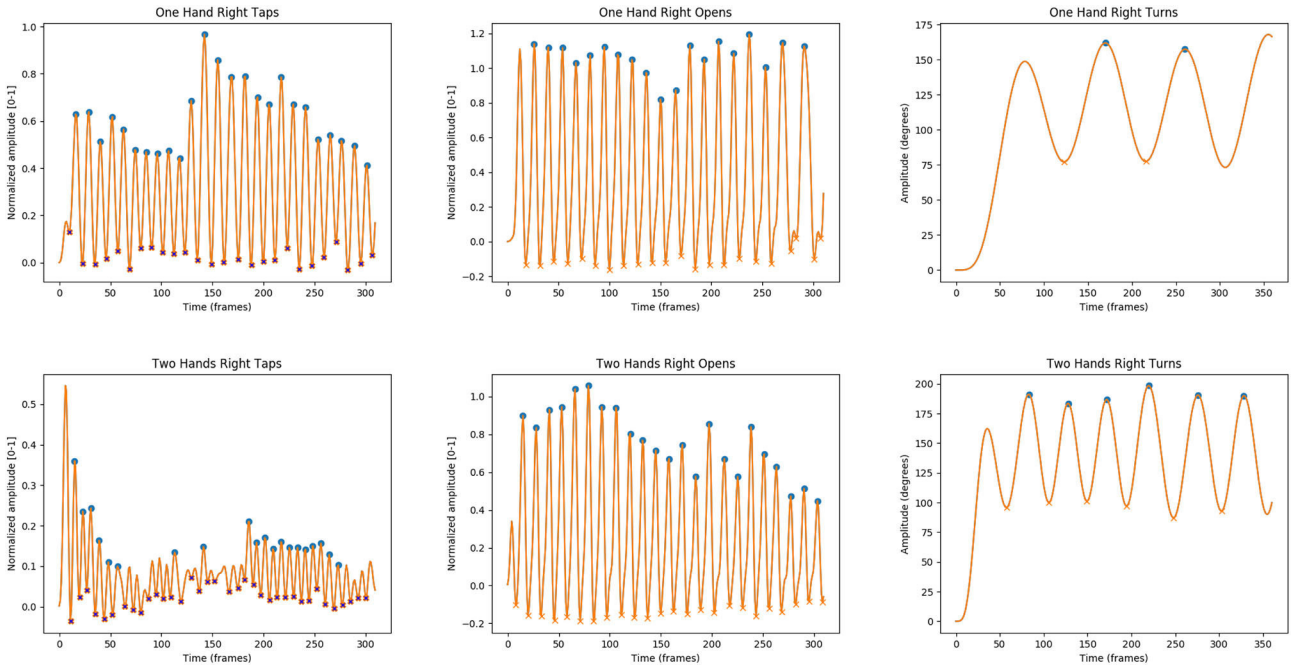

FIGURE 2 | Acceleration traces during the single-hand (unilateral) and two-hand (bilateral) motor tasks using the webcam. Representative segment of the kinematic signal reconstructed during unilateral **(upper)** and bilateral **(bottom)** motor tasks from finger tapping, hand movement, and pronation/supination movements of the hand in a patient with Parkinson's disease (PD). Note the general worse performance in the dual tasks shown in the lower part of the image when compared with the corresponding task perform with just one hand.

and the corresponding area under the curve (AUC) was used to compare the performance of the three candidate classifiers per classification task.

Validation Dataset

An external validation dataset included 12 videos (six videos from the patients with PD and six from HSs) recorded with the same protocol. We evaluated the extracted features from each hand in the single-hand tasks, and the extracted features from each hand in the two-hand tasks.

Statistical Analysis

We compared the demographic characteristics between the PD and HSs groups using Mann–Whitney's *U* non-parametric test (continuous) and the chi-square test (categorical). The extracted motor features from the videos of the finger tapping, hand movement, and pronation-supination movements of the hands stratified by side were compared between the PD and HSs groups using the non-parametric tests (Mann–Whitney test). Spearman's r correlations between the bradykinesia MDS-UPDRS-III sub-scores and the quantitative assessment methods were calculated. To rule out the confounding effects due to gender and hand size, we evaluated the performance of the classifiers on a strata containing only the male participants. The significance level was set at a 2-sided *P*-value of 0.05 and RStudio version 1.1.414 was used for the statistical analysis.

RESULTS

Cohort Characterization

Twenty-two patients with PD (median [range] age: 49.7 [46.8–62] years) and 20 age-matched HSs (age: 49.9 [43.5–50.9] years) were enrolled in the study. The demographic features of the PD and HSs are described in **Table 1**. The patients with PD had a median disease duration of 2.6 [1.57–3.8] years since diagnosis and a median MDS-UPDRS-III score in Off-state of 18 [14–33] points.

Quantitative Motor Assessment Using the Webcam

The single features extracted by the classifiers showed differences between the most affected side (MAS) and less affected side (LAS) in the patients with PD and between the dominant side (DS) and non-dominant side (NDS) according to handedness in HSs (**Table 2**). There were statistically significant differences for the unilateral finger tapping speed, hand movement speed, and pronation-supination movement amplitude ($P < 0.05$) (**Table 2**). For the bilateral task, there were statistically significant differences for the finger tapping amplitude, finger tapping speed, and hand movement speed ($P < 0.05$) (**Table 2**).

Concurrent Validity With MDS-UPDRS Part III Scores and Inertial Data

In the patients with PD, the video-extracted speed of the MAS showed significant moderate negative correlation with the MDS-UPDRS-III score of the MAS for hand movement ($r = -0.50$,

TABLE 1 | The demographic characteristics and clinical features of the patients with Parkinson's disease (PD).

		Parkinson's disease ($n = 22$)	Healthy subjects ($n = 20$)	*P*-value (PD vs. HS)
Baseline demographic characteristics				
Age, median (IQR)		49.7 (46.8–62)	49.9 (43.5–50.9)	0.21
Sex, *N* (%)	Man	16 (72.7)	6 (30)	0.01
	Woman	6 (27.3)	14 (70)	
Education, years median (IQR)		19 (17–20)	18 (16.7–20)	0.98
Laterality Preference Index (LPI)				
Handedness, *N* (%)	Right	19 (86.4)	20 (100)	0.48
	Left	2 (9.1)	0 (0)	
Parkinson's disease patients' characteristics				
Time since diagnosis (years), median (IQR)		2.6 (1.57–3.8)		
Predominant side at onset, *N* (%)	Right	17 (77.3)		
	Left	5 (22.7)		
Hoehn & Yahr stage, *N* (%)	Unilateral	19 (86.4)		
	Bilateral	3 (13.6)		
MDS-UPDRS III, median (IQR)		18 (14–33)		

$P < 0.05$). The video-extracted features showed correlation with objective quantification measures by IMU. Thus, the amplitude and the speed of movement of the MAS measured by the webcam showed significant moderate negative correlation with the corresponding MDRS-UPDRS-III bradykinesia item task measured by IMUs: finger tapping ($r = -0.59$, $P < 0.05$ and $r = -0.51$, $P < 0.05$ for amplitude and speed, respectively), hand movement ($r = -0.50$, $P < 0.05$; $r = -0.70$, $P < 0.05$), and pronation-supination movement of the hand ($r = -0.67$, $P < 0.05$; $r = -0.66$, $P < 0.05$).

Classification Performance of the Developed Model: Differentiating PD From HSs Using the Webcam

In the developed model, the features extracted from single-hand tasks (herein named unilateral) overall showed the highest classification performance compared with those using features extracted from the two-hand tasks (herein named bilateral). The unilateral classifiers showed the mean sensitivity and specificity values ranging from 41 to 73% and 23 to 80%, respectively, for all the three features, with a cross-validation AUC ranging from 0.35 to 0.81 (**Supplementary Table 1**). In the unilateral motor tasks, the combined right-left speed feature for finger tapping and hand movement and the variation in the amplitude for the hand movements and pronation-supination movements of the hand showed the highest values and consistency across the three different classifiers (**Supplementary Table 1**). In the bilateral motor tasks, the combined right-left amplitude for finger tapping, hand movement, and the combined right-left amplitude variability for hand movements and fatigue for the hand movements and pronation-supination movement of the hands showed the highest value and consistency across the three classifiers (**Supplementary Table 1**). The stratified analysis among the male participants showed a cross validation AUC ranging from 0.21 to 0.88. In the unilateral motor tasks, the combined right-left speed feature for finger tapping and hand movement and the mean amplitude and variation in the amplitude for the pronation-supination movements of the hand showed the highest values and consistency in the three different classifiers. Similar results were found for the bilateral tasks. The performance of classifiers can be found in **Supplementary Table 2**.

Validation of the Model on an Independent Dataset

When we applied our predictive model to an external validation dataset containing 12 videos (six PD and six HSs), in the unilateral motor tasks, the combined right-left speed for finger tapping, hand movement, and pronation-supination movement of the hand had the highest values and consistency across the three different classifiers, along with the combined right-left amplitude of the pronation-supination movement of the hand (**Table 3** and **Figure 3**). The AUC range for the Logistic Regression model in the unilateral finger tapping, hand movement, and pronation-supinations tasks ranged from 0.47 to 1, 0.28 to 1.00, and 0.40 to 0.94, respectively. For Naïve Bayes model, the AUC results for the unilateral tasks ranged from 0.47 to 0.83 in the finger tapping, 0.22 to 0.97 for hand grasp, and 0.41 to 0.89 in the pronation supination task. Finally, for the Random Forest model, the AUCs ranged from 0.41 to 0.75 in the finger tapping, from 0.49 to 0.78 in the hand grasp, and from 0.61 to 0.89 in the pronation-supination task (**Table 3**). For the bilateral motor tasks, the combined right-left amplitude for finger tapping, pronation-supination movement of the hand, and the combined right-left amplitude variability for hand movements and speed for pronation-supination movement of the hands showed the highest value and consistency across the three classifiers (**Table 3** and **Figure 3**).

TABLE 2 | Video-extracted motor features in the unilateral and bilateral tasks of the MDS-UPDRS-III bradykinesia upper limb motor tasks.

		PD		HS		
		MAS	**LAS**	**DS**	**NDS**	***P*-value**
Finger tapping						
Single hand (unilateral)	Amplitude Normalized amplitude [0–1]	0.73 (0.3)	0.81 (0.3)	0.84 (0.4)	0.87 (0.4)	0.345
	Speed (Time[frames])	2.03 (0.85)	2.26 (0.99)	2.35 (0.86)	2.19 (0.69)	0.247
	Fatigue	0.10 (0.27)	0.10 (0.27)	0.08 (0.15)	0.10 (0.19)	0.760
Two-hands (bilateral)	Amplitude Normalized amplitude [0–1]	0.56 (0.25)	0.77 (0.28)	0.79 (0.44)	0.80 (0.37)	0.042
	Speed (Time[frames])	2.13 (0.91)	2.25 (0.80)	2.03 (0.71)	2.03 (0.71)	0.705
	Fatigue	0.11 (0.20)	0.15 (0.25)	0.00 (0.33)	0.05 (0.33)	0.106
Hand movements						
Single hand (unilateral)	Amplitude Normalized amplitude [0–1]	0.92 (0.21)	0.97 (0.24)	0.9 (0.19)	1.02 (0.20)	0.904
	Speed (Time[frames])	1.40 (0.46)	1.80 (0.55)	1.68 (0.72)	1.58 (0.48)	0.143
	Fatigue	0.01 (0.18)	0.07 (0.18)	0.04 (0.16)	0.05 (0.19)	0.531
Two-hands (bilateral)	Amplitude	0.85 (0.25)	1.04 (0.27)	0.94 (0.15)	0.94 (0.15)	0.176
	Speed (Time[frames])	1.52 (0.41)	1.58 (0.46)	1.43 (0.41)	1.43 (0.41)	0.487
	Fatigue	−0.06 (0.17)	−0.01 (0.21)	0.11 (0.14)	0.09 (0.19)	0.044
Pronation supination movement of the hand						
Single hand (unilateral)	Amplitude (degrees)	116.67 (34.08)	137.21 (25.94)	136.18 (28.18)	120.72 (32.50)	0.053
	Speed (Time[frames])	1.55 (0.78)	1.78 (0.66)	1.65 (0.86)	1.54 (0.81)	0.698
	Fatigue	4.91 (24.01)	23.39 (36.64)	17.21 (53.79)	6.81 (39.19)	0.346
Two-hands (bilateral)	Amplitude (degrees)	113.07 (30.70)	130.50 (39.93)	128.45 (37.67)	129.85 (37.90	0.159
	Speed (Time[frames])	1.38 (0.46)	1.47 (0.47)	1.45 (0.69)	1.56 (0.70)	0.689
	Fatigue	21.94 (40.28)	4.88 (45.59)	28.39 (42.69)	2.00 (37.79)	0.622

Video-extracted motor features in the unilateral and bilateral tasks of the MDS-UPDRS-III bradykinesia upper limb motor tasks. PD, Parkinson's disease; HSs, healthy subjects; MAS, most affected side; LAS, less affected side; DS, dominant side; and NDS, non-dominant side.

DISCUSSION

In this study, we have proven the concept that the motor performance can be assessed objectively using a conventional webcam. We found differences in the motor performances between the different sides of the body and between the patients with PD and HSs in all the upper limb motor tasks used to evaluate bradykinesia. The best performing classifiers were unilateral finger tapping and hand movement speed achieving an almost perfect classification similar to other diagnostic tests in PD (21). In addition to this high classification performance, the model correlated both with IMUs for quantitative assessment of motor function and the most used standard MDS-UPDRS part III, hence demonstrating concurrent validity with the existing gold standard methods.

Video-Based Motor Evaluation

Different video-based systems have been described for the automated assessment of upper limb motor performance in the patients with PD (10). Most of these studies are restricted to the performance of one single motor task of the MDS-UPDRS-III with scarce comparisons of the motor performance between the different body sides (10, 11). Additionally, most of these systems have been traditionally used in a lab setting and have not yet been transitioned to the home setting (10, 22).

Recently, some video-based technologies have approached the study of motor performance using the low-quality video cameras. Using the smartphones cameras, different studies showed that it is possible to predict the presence of bradykinesia while performing the finger-tapping tasks, with an over 0.70 test accuracy, but with low discriminative capacity between the PD and HSs (23–25). Other studies, assessing the finger tapping

TABLE 3 | Model performance validation for PD classification.

Validation dataset		LR		NB		RF	
		AUC	**ACC**	**AUC**	**ACC**	**AUC**	**ACC**
Finger tapping							
Single hand	Amplitude_mean	0.472	0.333	0.583	0.500	0.458	0.500
(unilateral)l	Amplitude_std	0.583	0.500	0.472	0.500	0.458	0.417
	Speed	**1.000**	**1.000**	**0.833**	**0.667**	**0.750**	**0.667**
	Fatigue	**0.722**	**0.583**	**0.611**	**0.583**	0.417	0.500
Two-hands	Amplitude_mean	**0.777**	**0.750**	**0.750**	**0.500**	0.556	0.417
(bilateral)	Amplitude_std	0.444	0.500	0.500	0.583	0.597	0.583
	Speed	0.208	0.500	0.125	0.250	0.458	0.417
	Fatigue	0.500	0.416	0.222	0.500	0.556	0.500
Hand movements							
Single hand	Amplitude_mean	**0.639**	**0.667**	0.417	0.500	0.528	0.583
(unilateral)	Amplitude_std	0.278	0.500	0.222	0.333	0.486	0.417
	Speed	**1.000**	**1.000**	**0.972**	**0.917**	**0.778**	**0.583**
	Fatigue	0.472	0.417	**0.750**	**0.583**	0.556	0.583
Two-hands	Amplitude_mean	**0.750**	**0.667**	0.528	0.667	0.292	0.250
(bilateral)	Amplitude_std	0.472	0.500	0.528	0.417	**0.708**	**0.667**
	Speed	0.389	0.417	0.389	0.500	0.056	0.250
	Fatigue	0.333	0.417	0.500	0.417	0.569	0.583
Pronation-supination movement of the hands							
Single hand	Amplitude_mean	**0.917**	**0.667**	**0.778**	**0.750**	**0.667**	**0.417**
(unilateral)	Amplitude_std	**0.944**	**0.917**	**0.889**	**0.917**	**0.889**	**0.833**
	Speed	**0.750**	**0.750**	0.417	0.250	**0.611**	**0.667**
	Fatigue	0.444	0.417	**0.611**	**0.500**	**0.778**	**0.750**
Two-hands	Amplitude_mean	**0.833**	**0.750**	**0.861**	**0.833**	0.542	0.500
(bilateral)	Amplitude_std	**0.611**	**0.750**	**0.861**	**0.750**	**0.625**	**0.583**
	Speed	**0.611**	**0.583**	**0.750**	**0.750**	**0.750**	**0.750**
	Fatigue	0.306	0.333	0.583	0.583	0.306	0.500

Validation results of the combined right and left motor features for PD classification. The validation was made using three classifiers: Logistic regression (LR), Gaussian Naïve-Bayes (NB), and Random Forest (RF). Features with cross-validation AUC > 0.6 are highlighted in bold. Units: normalized amplitude [0–1] for finger tapping and hand movements; amplitude (degrees) for pronation supination for amplitude features. Time (frames), for speed in all the tasks. AUC, cross-validation area under curve; ACC, accuracy.

motor task with conventional webcams also showed similar results to our study (11, 22).

One of the most interesting aspects of this work is that the performance of the model was lower when we evaluated the different motor features extracted individually than when we integrated them. Specially, the inclusion of the side reflecting the asymmetry typical of PD increased the diagnostic performance dramatically and emphasized how critical the integration of information is for the clinical diagnosis.

The integration of information happens during a standard clinical evaluation. To evaluate a patient and establish a diagnosis, the neurologist needs to: (1) have a predefined criteria of average and non-average motor performance for each body side, (2) evaluate the different aspects of the motor performance (e.g., speed, amplitude, and fatigue), (3) compare the motor performance between each body side, (4) evaluate if the observed pattern matches the previous cases with the disease or that of the HSs. In our study, we replicated this behavior and trained a model that can recognize decrements in amplitude and speed of movement between the PD and HSs groups. This information was also combined with the motor performance asymmetry of one side compared with the other one. Thus, the accuracy obtained for some of the extracted motor features (i.e., finger tapping speed or hand grasp speed) could complement the one obtained from an expert neurologist (26). It is remarkable that the computer needed a 12 s video per task to perform a classification of PD vs. HSs based on the performance of bradykinesia tasks. Therefore, our method has many conceptual resemblances with the routine diagnostic process, making it interpretable and aligned with the standard of care, and supporting the potential of feature integration mimicking the behavior of the human brain.

Importantly, the system could also detect the differences in motor performance between the unilateral tasks and bilateral tasks, showing a worse performance when performing bilateral tasks in the group of patients with PD compare with HSs (**Table 2**). This is in line with the described impaired ability to perform the bilateral tasks, either simultaneously or sequentially, that occurs in the patients with PD. Thus, when performing a bilateral task, the motor performance in the patients with PD can

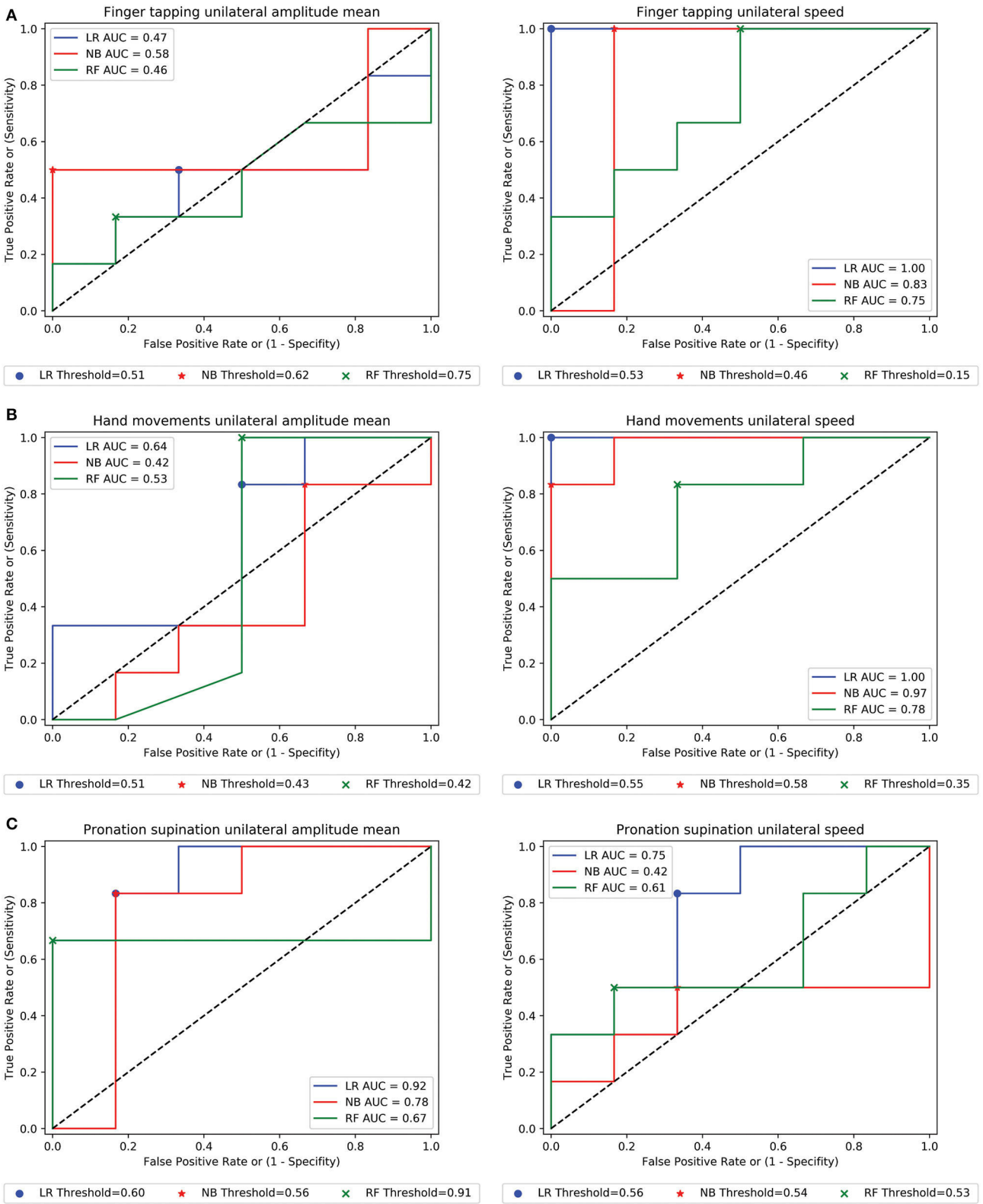

FIGURE 3 | The receiver operating characteristic (ROC) curves in the validation cohort. **(A–C)** Example of ROC curves of the combined right-left amplitude and speed of movement in the single-hand (unilateral) motor tasks for the three used classifiers for the patients with PD classification.

show a dramatic reduction in the movement of the most affected side compared to the unilateral tasks (27, 28).

This proof-of-concept study hence demonstrates that a standard webcam coupled with an artificial intelligence method has potential for accurately assessing upper limb bradykinesia in the patients with PD remotely. The camera employed for all the experiments was a webcam of standard laptop produced in 2010 (a 2010 MacBookPro). Any current laptop or mobile device allows video recording with a higher resolution and frame rate. This tool expands the portfolio of technologies available for evaluating the patients with PD, with the advantages of not needing any dedicated equipment outside of a standard laptop and using a video which also permits a simultaneous verification of the motor performance using the traditional clinical methods (i.e., the healthcare professional could review the raw video that generated the score when needed for quality control purposes). The most salient applications of this video-based technology could be the use in remote teleconsultations, which have surged with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic (29) and the decentralized clinical trials, as a complement for the standard assessments using MDS-UPDRS or other objective evaluation methods (i.e., sensors) (30, 31). In addition, this system could help minimize variability in clinical assessment in the clinical trials.

In this way, and in keeping with the previous initiatives (11, 22), we have recently developed a web app for the remote recording of the upper limb bradykinesia motor tasks. The app includes conformance statement signing, video instructions for every task, and the indications to facilitate hand positioning. Furthermore, it requires no software to be installed, thus using any standard laptop and any operating system. The upcoming studies will show the feasibility of its implementation for the assessment of the tasks in the at-home setting.

Limitations

Our work has several limitations. First, this is a proof-of-concept study with a reduced sample size, with specific disease characteristics (age and duration of disease), and the comparison was made only with healthy controls. Both the factors limit the generalizability of the results. Additionally, the study cohort is integrated by early patients with PD with predominant unilateral motor symptoms. Yet, this provides a convenient scenario to test the discriminative strength of the method. In the future, our results should be verified in larger cohorts with a representation of a broad spectrum of the patients with PD, such as the groups with different age and disease duration. In addition, the discriminative power of the method when including other parkinsonian syndromes in the mix remains to be established as well. Another limitation is that we restricted the assessment to the upper limb bradykinesia motor tasks of the MDS-UPDRS III. However, the motor performance of upper limbs is a predictive characteristic of onset and PD progression (32, 33). Therefore, its analysis is of the utmost relevance for the clinical evaluation and outcome of the patients with PD. The assessment of the global motor performance, such as lower limbs, and other disease manifestations, such as tremor, axial signs, and gait represents a future expansion of the current concept of objectively measuring other disease motor features using a standard video. This can improve the model performance and hence needs to be investigated. Finally, we focused our analysis on the evaluation of the binary classification performance of the present method. Future work should evaluate the additional quantitative aspects of the motor performance, increasing the granularity of the information, be able to rate the disease severity, and the detection of subtle changes in the motor status along the time, and after a therapeutic intervention. Those aspects will be critical for the application of this system in telemedicine and potentially clinical trials.

CONCLUSIONS

We proved the concept that a novel webcam-based technology can accurately evaluate bradykinesia, the single core feature that allows the diagnosis of parkinsonism, in a remote setting, using artificial intelligence. This method has an accuracy performance that could complement the usual diagnostic process performed by the experienced movement disorders specialists and could be easily expanded to other disease manifestations. Our results need to be confirmed in the larger studies, such as patients with other forms of parkinsonism, age groups, and disease status.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of HM Hospitales who approved the study protocol (Protocol Number: 18.05.1245-GHM). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

MHGM has contributed to the design of the solution, the recruitment and evaluation of the participants, the analysis of the data, and the manuscript draft. SD, JV-O, and NM have participated in the technology development, the analysis, and the draft of the manuscript. AA and TM have participated in the critical review of the project, evaluation of the results, and the manuscript elaboration. AS-F has contributed to the conceptualization of the solution, its development, the clinical validation, the draft, and the review of the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.742654/full#supplementary-material

Supplementary Figure 1 | Landmarks extracted for every hand by OpePose.

Supplementary Table 1 | Model performance training for Parkinson's disease (PD) classification. Classification results of the combined right and left motor features for PD classification prediction. The training of the model was made using three classifiers: Logistic regression (LR), Gaussian Naïve-Bayes (NB), and Random Forest (RF). Features with cross-validation AUC > 0.6 are highlighted in bold. Units: normalized amplitude [0–1] for finger tapping and hand movements; amplitude (degrees) for pronation supination for amplitude features. Time (frames), for speed in all tasks. AUC, cross-validation area under curve; ACC, accuracy.

Supplementary Table 2 | Model performance training for PD classification in men. Classification results of the combined right and left motor features for PD classification prediction. The training was made using three classifiers: LR, NB, and RF. The features with cross-validation AUC > 0.6 are highlighted in bold. Units: normalized amplitude [0–1] for finger tapping and hand movements; amplitude (degrees) for pronation supination for the amplitude features. Time (frames), for speed in all tasks. AUC, cross-validation area under curve; ACC, accuracy.

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Vestibular Rehabilitation Telehealth During the SAEA-CoV-2 (COVID-19) Pandemic

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During the COVID-19 pandemic, physical therapists transitioned to provide telehealth in the United States. We sought to determine the experiences of physical therapists delivering telerehabilitation for vestibular disorders including barriers, preferences, and concerns. A survey was created using the results of a focus group and previously published studies. The survey was distributed across social media sites and through email- the link was sent to the orthopedic, neurologic, and geriatric academies of the American Physical Therapy Association list serves. The email was also shared with each of the 50 state chapters of the American Physical Therapy Association. The survey was broken down into five sections: demographic information, physical therapists' general impressions of telehealth, physical therapists' comfort level treating various vestibular diagnoses, and common barriers physical therapists experienced during telehealth sessions. There were 159 completed surveys. More than 80% of physical therapists surveyed agreed that telehealth was an effective platform for vestibular physical therapy. When asked whether physical therapists felt the patient had similar health outcomes with telehealth versus clinic care 68% of physical therapists agreed. For the physical therapists who treated posterior or horizontal canal benign paroxysmal positional vertigo *via* telehealth, more than 50% were comfortable treating these conditions *via* telehealth. In analyzing common peripheral vestibular diagnoses treated *via* telehealth including bilateral vestibular loss, Meniere's disease, and vestibular neuritis more than 75% of the physical therapists reported comfort treating these diagnoses. Similarly, more than 75% of physical therapists who treated central vestibular diagnoses- including mild traumatic brain injury and vestibular migraine- *via* telehealth reported being comfortable treating these diagnoses. Physical therapists reported several barriers to tele healthcare ranging from concerns about testing balance with no caregiver present (94%) to challenges with providing a written home exercise program (33%). Physical therapists report that telehealth is a viable mechanism for providing rehabilitation for persons with balance and

vestibular disorders. For common diagnoses, most physical therapists were comfortable treating vestibular disorders *via* telehealth. While barriers remain including maintaining patient safety and being able to complete a thorough vestibular exam, telehealth for vestibular physical therapy services holds promise for the delivery of virtual care.

Keywords: vestibular rehabilitation, telehealth, dizziness, vertigo, balance, physical therapy

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, COVID 19) virus upended health care around the world and forever changed how patients converse with and receive care from providers (1, 2). Bruch et al. (2) reported that physicians and psychologists in Germany had a shift to more positive attitudes toward telehealth because of the COVID 19 pandemic. Many clinicians quickly learned to use novel platforms to virtually examine and treat their patients with vestibular disorders and modify how they conducted their physical examination (3). A consensus document that helps guide physician management of persons with acute dizziness provides guidance for history taking and conducting a virtual vestibular physical exam (3). Telehealth visits have successfully been used after otologic surgery safely by surgeons (4).

The vestibular examination generally requires that the clinician be near the patient to view eye movements (1, 5, 6). Physical therapists have attempted to determine the reliability of select internet-based evaluative measures for musculoskeletal conditions (7). In a systematic review and meta-analysis, Cottrell et al. (8) reported that telehealth for musculoskeletal conditions appears to be effective. During the typical physical therapist examination of persons with dizziness an extraocular eye movement examination, the head impulse test, the head shaking test, vestibular ocular cancellation, positional testing, assessment of nystagmus type and direction, and tests of balance are incorporated plus others (5, 6). With vestibular rehabilitation, van Vugt et al. (9) reported that internet based vestibular exercises for persons with chronic vestibular disorders was effective.

The number of telehealth visits with physical therapist exponentially increased during the first 9 months of the pandemic. In the United States, 41 of 50 states prior to the pandemic permitted some form of telehealth by physical therapists in 2018 (10), with 6 states still having no official telehealth legislation in 2021 (11).

The use of telehealth for persons with balance and vestibular disorders may make care more affordable and accessible (12). Persons with complex conditions could be seen by experienced vestibular physical therapists that are not available locally *via* telehealth (13). However, it is important to gain an understanding of which diagnostic conditions physical therapists feel most comfortable treating *via* telehealth. Therefore, the purpose of the study was to understand how vestibular physical therapy changed during the COVID-19 pandemic by transitioning to telehealth. The aims of the survey were to describe physical therapist's general impressions of telehealth, which patient diagnoses physical therapists were comfortable treating, which examination techniques and exercises the physical therapists utilized, and what physical therapists considered as barriers to telehealth.

MATERIALS AND METHODS

Prior to the drafting of the Qualtrics survey (Qualtrics, Provo, UT) a review of the current literature on rehabilitation services *via* telehealth was completed. Dahl-Popolizio et al. (14) survey on the provision of occupational therapy experiences during the COVID-19 pandemic was reviewed prior to the development of the physical therapist survey. To determine the categories of questions to ask physical therapists, a focus group of four full time practicing physical therapists with experience delivering vestibular physical therapy *via* telehealth were queried. From the focus group, several themes were determined to be important concepts worth investigating i.e., comfort level with various diagnoses, barriers to treatment.

There were 70 questions broken down into five sections (see **Appendix A** in Supplementary Material for full survey) to the survey: general impressions about telehealth, comfort level with various diagnoses, examination procedures and exercise usage, barriers to telehealth, and demographic information. At the beginning of the survey, general questions about impressions of the use of telehealth for the delivery of vestibular physical therapy were asked. Physical therapists were asked whether they thought telehealth was an effective platform for delivery of vestibular physical therapy, whether they experienced differences in attendance for scheduled sessions, and whether they believed the patient had a similar health outcome compared with clinic care. Physical therapists were asked to rank their agreement with the survey statements about different diagnoses using a 5-point Likert scale: strongly agree, somewhat agree, neither agree nor disagree, somewhat disagree, and strongly disagree.

Demographic information included age, gender, years of vestibular physical therapy experience, years of telehealth experience, and their primary physical therapy practice clinical location.

Participants were asked if they had treated various vestibular peripheral and central pathologies *via* telehealth including the following diagnoses: Benign paroxysmal peripheral vertigo (BPPV) of the posterior, horizontal, and anterior semicircular canal, bilateral vestibular loss, cerebellar degeneration, Chiari malformation, mild traumatic brain injury (concussion), disequilibrium of aging, labyrinthitis, Mal de Debarquement, Meniere's disease, multiple sclerosis, persistent postural

perceptual dizziness, stroke (anterior or posterior inferior cerebellar artery), vestibular migraine, vestibular neuritis, and vestibular schwannoma. If "yes" was selected for either of these diagnoses, participants then completed a 5-point Likert scale rating how comfortable they were treating those diagnosis *via* telehealth: extremely comfortable, somewhat comfortable, neither comfortable nor uncomfortable, somewhat uncomfortable, and extremely uncomfortable.

Participants were asked about whether they were confident with the knowledge generated from various examination techniques and with certain exercises. A list of commonly used tests and measures were provided, listed in **Tables 2A,B** and **Appendix A** in Supplementary Material. The physical therapist marked all that they felt they were able to effectively provide *via* telehealth. The survey included a free text option for the participant to write in items not included on the provided list of examination procedures and exercises. Similarly, a list of commonly prescribed vestibular exercises was provided, and the participant marked those exercises they felt were effective to deliver *via* telehealth.

For the barriers faced during the telehealth visits section, participants were asked to rate on a 5-point Likert scale how often they experienced the barrier including: always, most of the time, about half of the time, sometimes, or never. Data were sub-categorized into "never" or "that they experienced some barrier."

The survey was disseminated using Qualtrics software and was approved by the Biomedical IRB of the University of Pittsburgh in Pittsburgh PA, USA. Distribution of the survey occurred through posts on social media sites and email. The email with the survey link was shared with the list serves of the neurologic, geriatric, and orthopedic academies of the American Physical Therapy Association (APTA). The link was also shared with every state physical therapist professional association. Additionally, six state physical therapist associations sent email blasts seeking participation. All completed survey participants acknowledged consent by completing the survey. The survey was open from March 2021–May 2021, since this survey was anonymous there was no follow-up completed.

RESULTS

One hundred ninety-eight physical therapists completed the survey with 159 surveys analyzed. Forty-one surveys were incomplete and thus were not included in the final analysis. It was not possible to save the survey once it was started, and therefore any incomplete surveys were removed to ensure no one person was represented more than once in the data. One hundred and fifty-nine surveys were analyzed and described with frequencies and percentages. **Table 1** shows the demographic information of the respondents including gender, age, and primary location where the physical therapists work. Two subgroups were determined based on years of vestibular experience- 0–10 years of vestibular experience ($n = 90$) and 15+ years of vestibular experience ($n = 28$). Both subgroups demographic information is listed in **Table 1**.

TABLE 1 | Demographic data from the physical therapist who completed the telehealth survey.

	Total responses $N = 159$	Therapists with 0–10 years' experience $N = 90$	Therapists with 15+ years' experience $N = 28$
Gender			
Female	133 (84%)	83 (92%)	25 (89%)
Male	22 (14%)	6 (7%)	1 (4%)
Prefer not to say	4 (2%)	1 (1%)	2 (7%)
Age			
20–34	58 (36%)	58 (64%)	–
35–54	82 (52%)	32 (36%)	9 (32%)
55–85+	19 (12%)	–	19 (68%)
Primary location where physical therapist worked			
Outpatient clinic	135 (85%)	81 (90%)	23 (82%)
Home health	6 (4%)	2 (2%)	3 (10%)
Skilled nursing facility	2 (1%)	1 (1%)	–
School based	2 (1%)	1 (1%)	–
Acute care/hospital	4 (3%)	2 (2%)	1 (4%)
Other*	10 (6%)	3 (4%)	1 (4%)

*Other includes research clinic and academic settings.

Participants responses to general impressions are listed in **Figure 1**. **Figure 1A** shows the percentage of agreement among participants as it relates to if they felt telehealth was a viable platform for physical therapy services. **Figure 1B** shows the percentage of agreement as it relates to session attendance and **Figure 1C** shows the percentage of participants who agreed telehealth produced similar outcomes to face-to-face clinic care.

In the survey pertaining to various diagnoses seen *via* telehealth, 17 diagnoses were included. Of the 17, the seven mostly commonly seen diagnoses in vestibular clinics were further assessed. The seven diagnoses were chosen based on the frequency that physical therapists treated the condition *via* telehealth. The responses were separated into two groups based on years of vestibular experience- 0–10 years vestibular experience ($n = 90$) and 15+ years of vestibular experience ($n = 28$). **Figure 2** shows the ratings of perceived comfort a physical therapist had if they treated someone with posterior canal BPPV (**Figure 2A**) or horizontal canal BPPV (**Figure 2B**) *via* telehealth. **Figure 2** shows responses to three commonly treated peripheral diagnoses. **Figure 3** illustrates the responses of physical therapists self-reported comfort level treating bilateral vestibular loss, Meniere's disease, and vestibular neuritis *via* telehealth. **Figure 4** illustrates the responses of physical therapist's self-reported comfort level to common central nervous system vestibular pathologies, vestibular migraine and mild traumatic brain injury.

Along with diagnoses, respondents were asked to rate if they could effectively complete components of the vestibular examination and various vestibular exercises *via* telehealth. The percentage of respondents who felt they could effectively conduct vestibular exam techniques *via* telehealth is included in **Table 2A** ($n = 159$). **Table 2B** shows the percentage of respondents who felt they could effectively provide vestibular exercises *via* telehealth ($n = 159$).

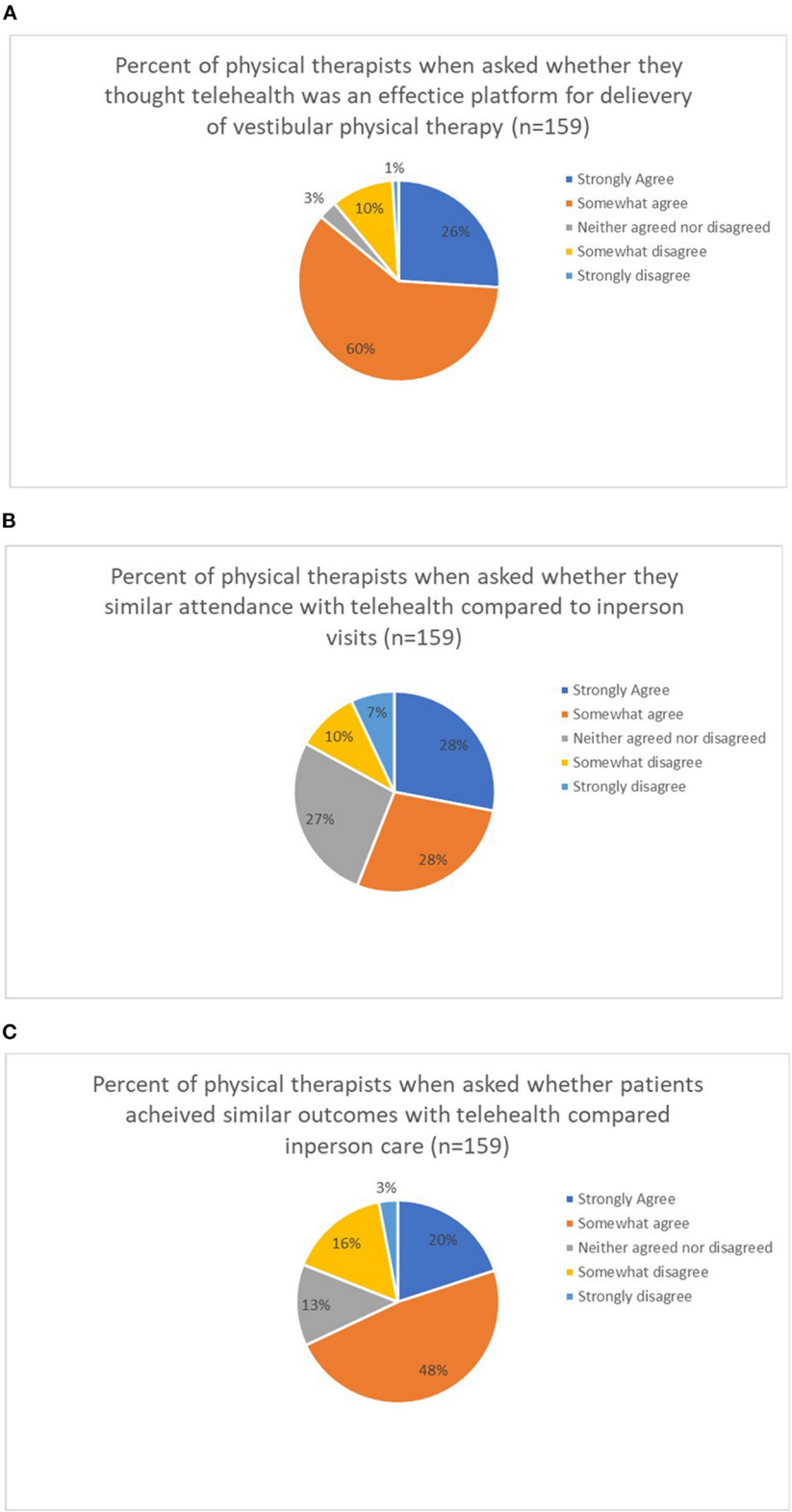

FIGURE 1 | (A–C) Percentage of agreement from physical therapists on general impressions of telehealth physical therapy for vestibular physical therapy services.

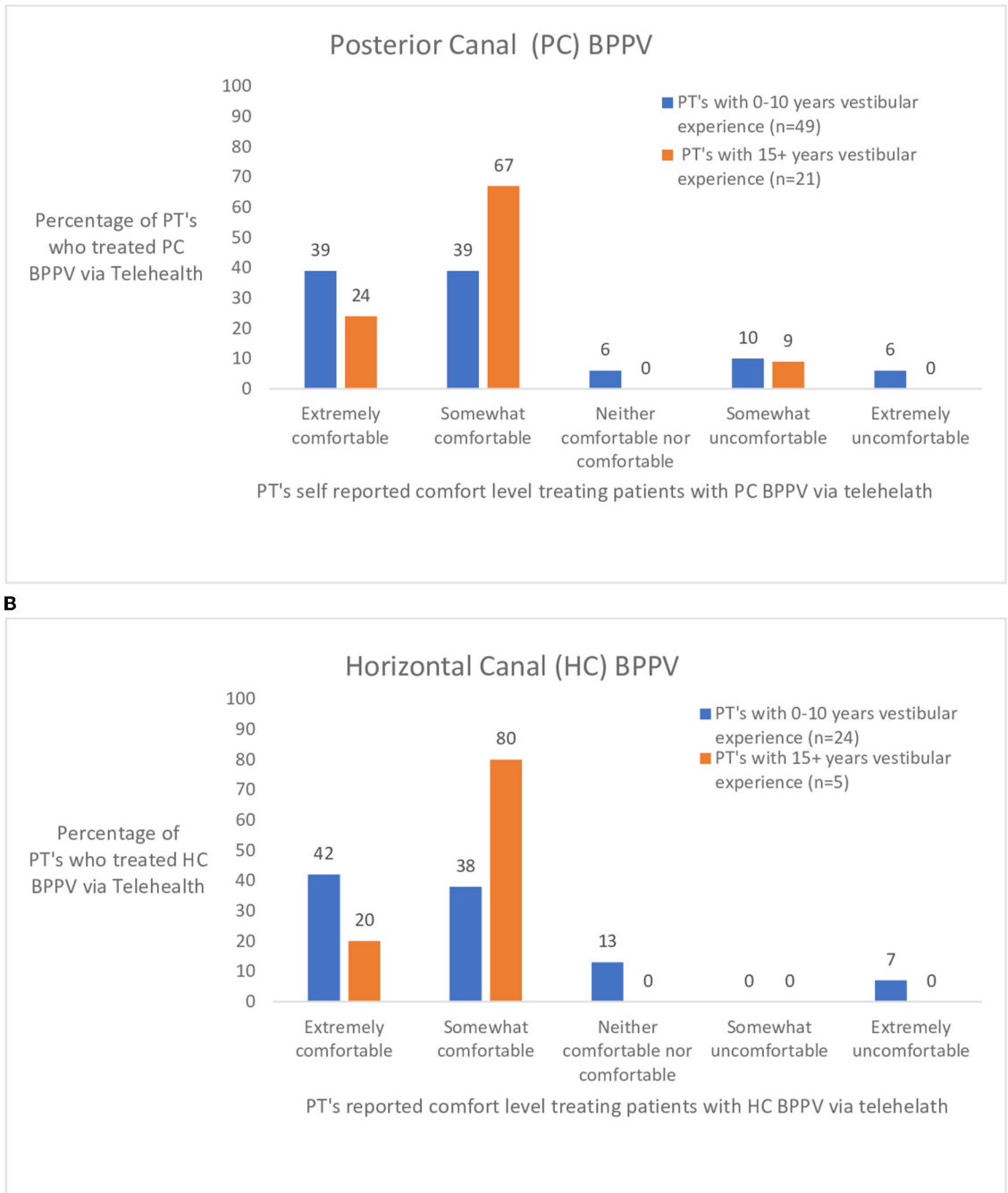

FIGURE 2 | (A,B) Rating by physical therapists (PT's) with 0–10 and 15+ years of vestibular experience who treated persons with posterior (PC) and horizontal canal (HC) benign paroxysmal positional vertigo (BPPV) *via* telehealth.

The final section of the survey included barriers physical therapists experienced during telehealth sessions. **Table 3** lists the percentage of physical therapists who rated that they experienced the barrier either always, most of the time, about half of the time, or some of the time ($n = 159$). The last question on the survey was "Do you have a sense that your telehealth visits were as effective as in-person visits?" and the results are shown in **Figure 5**.

DISCUSSION

Demographics

The number of physical therapists in the United States who treat persons with vestibular disorders *via* telehealth is unknown. Werenke et al. (15) reported that 37% of their physical therapists from their outpatient clinics ($n = 222$, 680 patients) provided

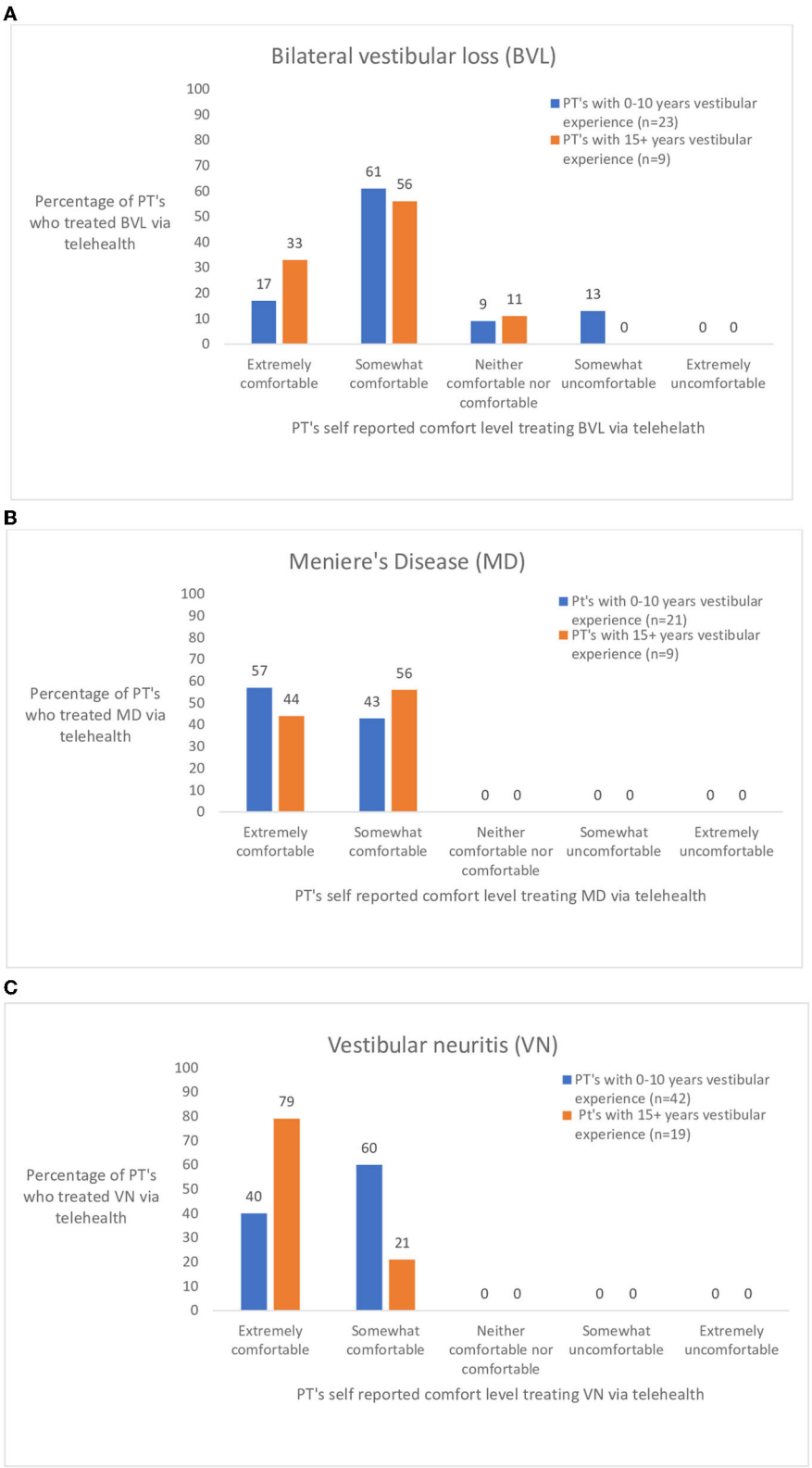

FIGURE 3 | (A–C) Ratings by physical therapist (PT's) with 0–10 and 15+ years of vestibular experience who treated persons with common peripheral vestibular diagnoses: bilateral vestibular loss (BVL), Meniere's disease (MD), and vestibular neuritis (VN) *via* telehealth.

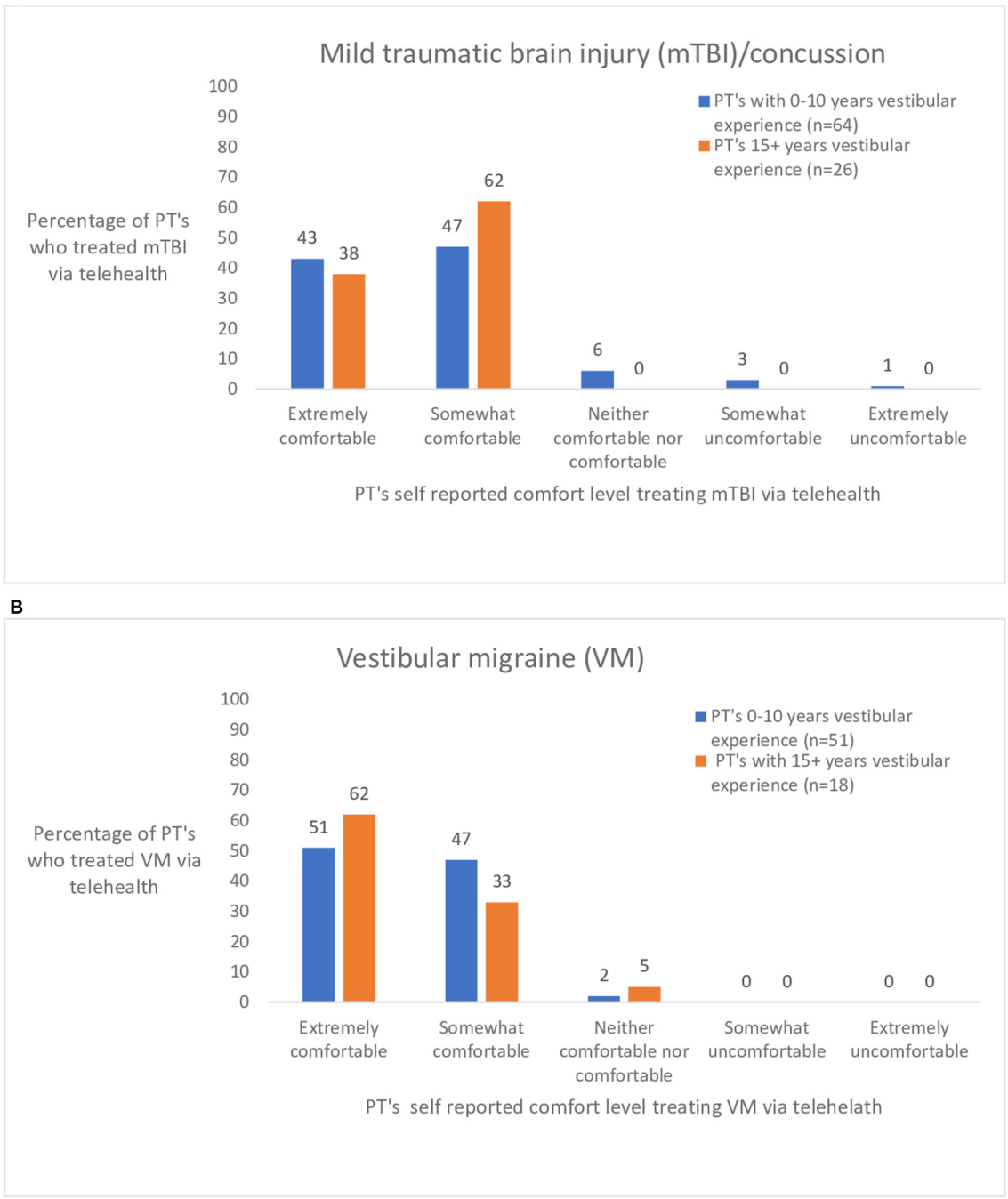

FIGURE 4 | (A,B) Ratings by physical therapists (PT's) with 0–10 and 15+ years of vestibular experience who treated persons with common central vestibular diagnoses: mild traumatic brain injury/concussion (mTBI) and vestibular migraine (VM) *via* telehealth. visits were as effective as in-person visits?" ($n = 159$).

telehealth care during the second and third quarters of 2020. There are 1,589 members of the Neurology Academy's Vestibular Special Interest (VSIG) group (personal communication, Sara Oxborough, 9/7/2021), but not all VSIG members treated persons *via* telehealth. It is unclear how many of the subjects were recruited from the VSIG vs. from other recruitment mechanisms.

Most of the respondents (66%) had between 6 months to 1 years' experience treating persons *via* telehealth with only 8% having >2 years of experience. Eighty-three percent of the physical therapists had 15 or less years of experience. It is unclear how many physical therapists were required to use telehealth technology to conduct telehealth visits.

Werneke et al. reported that patients who received physical therapy care *via* telehealth were younger and were more likely to live in a metropolitan area (15). The use of technology is a consideration for both the patient and the physical therapist.

TABLE 2 | (A,B) Percentage of physical therapist respondents who reported that they could effectively provide vestibular examination techniques and specific exercises *via* telehealth ($n = 159$).

	Number (Percentage) of respondents
Examination	
Cervical range of motion	137 (86%)
Symptom provocation with VORx1	132 (83%)
Smooth pursuit	125 (77%)
Romberg testing	118 (74%)
Saccades	118 (74%)
Home environmental assessment for safety	102 (64%)
Observation of nystagmus in room light	94 (59%)
VOR cancellation	92 (58%)
Clinical test of sensory integration and balance	85 (53%)
Vergence	84 (53%)
Cranial Nerve Function (3,4, & 6)	81 (51%)
Dix Hallpike	81 (51%)
Head shake test	25 (42%)
Hearing screen	25 (42%)
Dynamic visual acuity	25 (42%)
Roll test	62 (39%)
Dynamic gait index	53 (33%)
Cover/uncover test	51 (32%)
Cross cover test	42 (26%)
Gait speed	41 (26%)
Other*	16 (10%)
Sensory testing	14 (8%)
Head impulse test	10 (6%)
Exercise	
Habituation exercises	149 (94%)
Standing balance exercises- flat surface	147 (93%)
VORx1	147 (93%)
Walking with head turns side to side	121 (76%)
Gaze shift between two targets	118 (74%)
Walking with head turns up/down	114 (72%)
Standing balance exercises- complaint surface	101 (64%)
Saccades	97 (61%)
VORx2	82 (52%)
Walking with dual task	72 (45%)
Walking with quick turns	67 (42%)
Virtual reality exercises	67 (42%)
Remembered or imaginary target exercise	63 (40%)
Walking with eyes closed	39 (25%)
Walking with an obstacle course	35 (22%)
Walking on uneven surfaces	35 (22%)

**Other includes assessing for ataxia on finger to nose testing and testing for rapid alternating movement.*

TABLE 3 | Barriers physical therapists reported when completing telehealth vestibular therapy sessions.

Barrier physical therapist encountered during telehealth visit	Number (Percentage) of physical therapist responding
Concerns about testing balance with no caregiver present	149 (94%)
Bad/inconsistent internet signal	146 (92%)
Equipment set up limiting ability to view patient' body during exam or intervention?	146 (92%)
Patients were not familiar with how to use technology platform	141 (89%)
Difficulty walking with their telecommunications device	130 (82%)
Patient/client had technology incompatible for the visit	125 (79%)
Lack of a caregiver in the home	124 (78%)
Concerns about testing balance with a caregiver present	117 (74%)
Lighting- glare on glasses during the eye exam	104 (66%)
Challenging to provide a written home exercise program	52 (33%)

All responses except "never" included in the reported percentage below ($n = 159$).

Sixty-four percent of our physical therapist sample were ≥35 years of age, suggesting that physical therapists were able to adapt to telehealth platforms and the technology requirements to treat patient's virtually (see **Table 1**). Outpatient physical therapist practices were the most common practice setting (85%), which is not surprising since outpatient practices are the most common employment setting for physical therapists in the US (16).

General Impressions About Telehealth

Eighty-six percent of the physical therapist respondents felt that telehealth was effective for the delivery of vestibular physical therapy. Cottrell et al. have suggested that telehealth can be effective for the treatment of musculoskeletal conditions (8). Others have reported that patients ($n = 222{,}680$) were satisfied with their out-patient care for both orthopedic, non-orthopedic, and vestibular physical therapy care *via* telehealth (15). Per their study, the satisfaction ratings of persons seen in the clinic was only 3% higher than those who were treated *via* telehealth (15). Others have reported a 95% patient satisfaction rating in persons seen in outpatient rehabilitation locations (17). Our result of physical therapist satisfaction with telehealth mirrors the satisfaction of patients with their care.

Fifty-six percent of the physical therapists thought that there was enhanced attendance at physical therapy sessions *via* telehealth. Others have reported that attendance might be positively affected with the use of telehealth (18).

Related to whether physical therapists thought that the patient achieved similar outcomes, 68% agree and 19% disagreed and felt that the outcomes were not as good with telehealth. The 19% who reported that they felt that patient had worse outcomes might be related to bandwidth and connection issues, issues related to patients having difficulty with their telecommunication devices, and resistance to change (18).

Comfort Level With the Diagnoses Seen in Vestibular Physical Therapy *via* Telehealth

BPPV is the most common condition seen in vestibular clinics (19). Physical therapists were generally comfortable using telehealth to treating persons with posterior and horizontal canal BPPV as described by Barreto and Yacovino (1). Barreto and Yacovino (1) utilized cell phones to observe eye movements during the Dix-Hallpike and the roll test. They suggested that it is imperative to utilize telecommunication devices that incorporate both audio and video in the examination and treatment of persons with BPPV *via* telehealth.

However, there were both experienced and less experienced physical therapists who were uncomfortable treating posterior or horizontal canal BPPV *via* telehealth. The survey question did not ask about what lead the physical therapist to be uncomfortable. A possible scenario could be whether the patient had a caregiver at home to assist in the telehealth visit which may have modified their responses as to their level of comfort in treating persons with BPPV.

Persons with BPPV can experience a Tumarkin like event upon resuming the sitting position during the treatment of posterior canal BPPV (20). With older persons, it may be important to have an additional person in the home to avoid a fall after the repositioning maneuver. Barreto and Yacovino suggest that the diagnosis can be made *via* telehealth first, followed by a decision to treat *via* telehealth or in the clinic (1). Clinicians may be more willing to treat persons with BPPV who have previously experienced BPPV in the past (1), as voiced during the focus group meeting. If the person's BPPV symptoms do not resolve with telehealth visits, Shaikh et al. suggest that persons be seen in the clinic (3).

The number of people reporting that they had treated persons with bilateral vestibular loss (BVL) was low and most reported that they were "somewhat comfortable" treating persons with BVL. It is known that persons with BVL fall frequently (21), thus care is required with challenging balance activities in the home.

Unlike BVL, all physical therapists were comfortable with treating persons with Meniere's disease and vestibular neuritis. These two diagnostic groups of the 7 discussed were the only diagnoses where all respondents felt comfortable treating *via* telehealth.

The pandemic reduced sports related concussions by 60% (22). Persons with mild traumatic brain injury were treated later by an average of 26 days compared to pre pandemic time from accident to presentation to the clinic (22). Thus, persons with mild traumatic brain injury seen during the pandemic *via* telehealth may have been more chronic in our survey as well. Generally, participants were comfortable treating persons with mild traumatic brain injury and vestibular migraine *via* telehealth. It may be more difficult to determine if persons post pandemic with mild traumatic brain injury will respond to physical therapy *via* telehealth in a similar manner to those who were seen during the pandemic because of the differences in chronicity.

Overall, physical therapists were comfortable with treating vestibular migraine *via* telehealth.

Examination Procedures

Per **Table 2A**, our respondents did not believe that all examination techniques could be effectively administered *via* telehealth. Items endorsed by <30% of the respondents included the cross-cover test, gait speed, coordination testing, sensory testing, and the head impulse test. Green et al. (23) suggested that tests of skew and the alternate cover test could be performed *via* a virtual exam with a cell phone. They suggest that the head impulse test can be performed with active participation of the patient under the direction of the clinician to implement the head impulse test (23). No data is provided to report the reliability or validity of testing the test of skew, nystagmus or head impulse test *via* telehealth (23). The telehealth exam may be hampered by an inadequate frame rate, the ability of the patient or caregiver to hold the phone in the correct position with adequate light to visualize the eyes, or an unstable internet signal (1, 23, 24).

Recording gait speed is a challenge as it is often impossible to accurately determine distances in a person's home to calculate velocity. With cell phones or other technologic devices, it may be difficult to assess coordination and timing of both upper and lower extremity movements.

Sensory testing is a challenge *via* telehealth, yet sensory testing is a vital aspect of the exam that can help guide which balance tests can be performed safely. With loss of distal sensation, performing the Romberg test with eyes closed while a person holds a telecommunication device would not be advised.

Forty-eight percent of the examination procedures utilized in telehealth were rated as not being effective by the physical therapists. There is much work that needs to be done to improve the use of examination procedures commonly utilized by physical therapists in the assessment of persons with balance and vestibular disorders *via* telehealth.

Exercise in the Home *via* Telehealth

The use of exercises (see **Table 2B**) had higher efficacy ratings by the physical therapists when compared to the overall ratings of the examination procedures in **Table 2A**. Although most exercises were endorsed as being able to perform in the home, challenging gait exercises, virtual reality exercises and the remembered or imaginary target exercises had the lowest confidence ratings by the physical therapists. The eye exercises were rated at 50% or greater except for the remembered or imaginary target exercise, which is often difficult to teach and challenging for patients to remember how to perform the exercise correctly regardless of setting.

Participants may have rated the gait exercises low for fear of the patient falling, the difficulty locating a walkway in the home

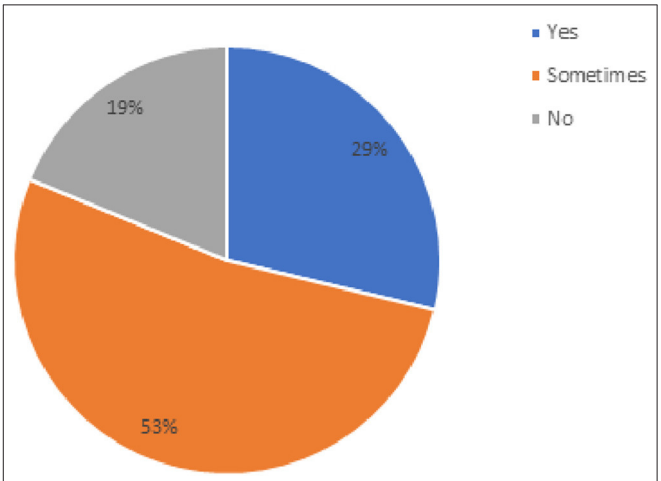

FIGURE 5 | Percentage of physical therapists' responses when asked about "do you have a sense that your telehealth visits were as effective as in-person visits?" ($n = 159$).

where the device can transmit their gait clearly, or the lack of a caregiver to guard the patient while performing the exercises. It will remain challenging to work on advanced postural skills during gait without having someone nearby to guard the patient. Making decisions to progress based on performance may also be challenging because small nuances in postural control may not be easy to visualize over a telecommunication device. However, remote cell phone monitoring is being done and demonstrates promise in enhancing decision making about fall risk (25, 26). The in-home utilization of cell phones to monitor sit to stand abilities and walking will assist in future telehealth decision making (25, 26). In summary, examination of the client in the home appears to be more challenging than providing exercises for rehabilitation *via* telehealth.

Barriers to Telehealth

As reported in **Table 3**, the primary concern was treating the patient without a caregiver present followed by an inconsistent internet signal and the ability to see the correct body part to make a sound clinical judgement (3, 12). Others have reported that familiarity with the use of technology is a barrier, as did our respondents (18). There were concerns about the ability of persons to walk with a telecommunication device if their gait was impaired and concerns about a person's balance. The other concern was that with the lighting (too much or too little) the physical therapist was challenged in conducting an adequate exam to make clinical decisions (3). Although not asked in our survey, persons who are hearing challenged may have more difficulty communicating *via* telecommunications (12, 27) and is something to consider with persons with both vestibular and audiologic impairments.

Only 29% of the physical therapists felt that telehealth was as effective as in person care (see **Figure 4**). With enhanced video streaming, greater comfort with the technology, and virtual mechanisms to better assess posture and gait, these effectiveness ratings may improve with time.

Limitations

The survey was active during March-May 2021. It is impossible to know how robust our response rate was since it is unknown how many physical therapists in the United States treated persons *via* telehealth with balance and vestibular disorders. The response rate of 198 is most likely low. However, Dahl-Popolizio et al. (14) had 230 surveys returned about occupational therapists' experiences with telehealth from 137,000 members. The study was mainly distributed through state chapters, academies of the American Physical Therapy Association and social media. Our methods of survey distribution may have limited access to the survey and could have potentially biased sample. Another limitation to the study includes the inability to complete any follow-up after the initial survey. We were unable to determine if physical therapist's perception of telehealth during the pandemic changed as the pandemic progressed.

Only 8% of the respondents had 2 years or more of experience conducting telehealth visits, yet most of the physical therapists were positive in their responses. It is possible that only those physical therapists who liked performing telehealth visits responded to the survey request biasing the findings. Not all out-patient physical therapists performed telehealth during the shutdowns in the United States (15). It appears that some form of telehealth will continue in most areas of the world long after the pandemic has stabilized (28–34).

The Future of Telehealth With Vestibular Physical Therapy

It appears that there is a promising future for the telehealth delivery of vestibular physical therapy. Improved technology may assist with some of the technological issues revealed by this study (i.e., eye movement examination). The assessment of balance and postural control will be a more challenging issue for telehealth users, although with recent advances in technology the examination of postural control and gait is improving. Developing guidelines or rules to help determine when it is safe to test people in challenging positions will need to be determined and shared to prevent falls during telehealth visits. Overall physical therapist satisfaction appeared high with telehealth, yet physical therapists continued to feel that person to person visits yielded more effective visits.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by STUDY21020099. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.781482/full#supplementary-material

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Eye and Head Movement Recordings Using Smartphones for Telemedicine Applications: Measurements of Accuracy and Precision

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Objective: Smartphones have shown promise in the assessment of neuro-ophthalmologic and vestibular disorders. We have shown that the head impulse test results recorded using our application are comparable with measurements from clinical video-oculography (VOG) goggles. The smartphone uses ARKit's capability to acquire eye and head movement positions without the need of performing a calibration as in most eye-tracking devices. Here, we measure the accuracy and precision of the eye and head position recorded using our application.

Methods: We enrolled healthy volunteers and asked them to direct their eyes, their heads, or both to targets on a wall at known eccentricities while recording their head and eye movements with our smartphone application. We measured the accuracy as the error between the eye or head movement measurement and the location of each target and the precision as the standard deviation of the eye or head position for each of the target positions.

Results: The accuracy of head recordings (15% error) was overall better than the accuracy of eye recordings (23% error). We also found that the accuracy for horizontal eye movements (17% error) was better than for vertical (27% error). Precision was also better for head movement (0.8 degrees) recordings than eye movement recordings (1.3 degrees) and variability tended to increase with eccentricity.

Conclusion: Our results provide basic metrics evaluating the utility of smartphone applications in the quantitative assessment of head and eye movements. While the new method may not replace the more accurate dedicated VOG devices, they provide a more accessible quantitative option. It may be advisable to include a calibration recording together with any planned clinical test to improve the accuracy.

Keywords: eye tracking, smartphone, ARKit, neurologic examination, stroke, vertigo

INTRODUCTION

Abnormal eye movements are observed in a variety of neurological diseases, such as stroke, ataxia, and cranial nerve damage (1). A thorough and precise analysis of eye movements can potentially provide key information regarding the affected structures (2). Examination of eye movements is quick and non-invasive and can aid the diagnosis (3). Furthermore, there are examples of eye movement examination batteries, such as the Head Impulse test, Nystagmus, Test of Skew (HINTS) exam, that have been shown to be more sensitive than MRI in diagnosing stroke in dizzy patients (4).

Despite the benefits of examining eye movements in the clinical setting, there are barriers to the widespread use of these examinations. For example, detection and interpretation of eye movements may require clinical expertise; the abnormalities may be subtle and hard to recognize with naked eyes; and sometimes quantitative measurement of eye movements is needed in order to reach a clinically meaningful conclusion (3). To overcome these barriers, video-oculography (VOG) goggles were used to objectively measure the eye movements in clinical settings (3, 5, 6). VOG has the potential to provide diagnostic clues in various clinical settings, such as emergency departments, primary care, or even patients' homes. VOG goggles are not readily available everywhere, however, due to the cost and the lack of expertise to use them and interpret their results.

Recent developments in the consumer market have introduced eye-tracking technology to common smartphones. This provides an opportunity to improve accessibility to eye movement testing technology on a broader scale. There has been more attention to the gaze tracking features of smartphones recently (7). A few studies have evaluated the accuracy of gaze tracking using smartphones and have shown acceptable findings (8–10).

In 2020, Greinacher and Voigt-Antons investigated the accuracy of eye tracking based on ARKit, Apple's eye, and face-tracking framework (11). They found that the accuracy of eye tracking based on the ARKit framework provides comparable results to methods investigated on other smartphones, tablets, and cameras (11). In a recent study, we introduced a smartphone application that quantifies one of the most common tests of vestibular function, the head impulse test also using Apple's ARKit framework (12).

In our previous study, we found that eye movement data recorded by the iPhone matched reference standard portable VOG goggles, qualitatively. However, quantitatively, the results were correlated but not exactly replicated (12). To address this observation, we need to further look into the characteristics of the recordings using the ARKit framework and the potential value of introducing a calibration produce. Calibration procedures are common in most eye-tracking devices (7) as they need to adapt to the physical characteristics of each person to produce accurate results. Thus, we need to understand whether the smartphone too could potentially benefit from a battery of tests that calibrate it prior to testing. In this study, we aimed to evaluate the precision and accuracy of eye and head position measurements using our developed application.

METHODS

Participants

We recruited 12 healthy volunteers for this study (mean age: 41 ± 5; range: 23–69). The inclusion criteria were defined as not having known disease affecting the eye movements, being able to maintain a sitting position for the duration of the test (≈1–1.5 h), and having intact visual fields. The experiments were explained to the participants prior to testing and written informed consents were obtained. The study protocol was reviewed and approved by the local institutional review board (IRB00258938).

Experimental Setup

Participants sat in a chair 1 m away from a central target placed at eye level on the wall. We placed targets on the wall in the horizontal plane at 5 degrees left & right from center (8.75 cm), 10 degrees (17.5 cm), 15 degrees (26.25 cm), and 25 degrees (43.75 cm). We also placed targets on the wall in the vertical plane. We placed markers on the wall in the vertical plane at 5 (8.75 cm) degrees from center, 10 (17.5 cm) degrees and 20 degrees (35.0 cm) in the upward and downward directions. The range was smaller in the vertical plane due to the inherently more restrictive nature of movements in the vertical plane vs. the horizontal plane.

We developed an application with ARKit running on an iPhone 12 pro (Apple Inc., Cupertino, CA, USA)[1] to record both eye and head movements (12). ARKit provides continuous recordings of both eye and head positions at 60 samples *per second* using the front-facing combination of infrared and natural light cameras and sensors. We also made use of a custom timer to standardize intervals between eye and/or head movements. Lastly, we used a head-mounted laser to ensure the head was pointing at the correct target in the tests that involved head movements.

The smartphone used to record the data was mounted on a tripod at a distance of 25–40 cm away from the patient's face—but at a slight offset so as to not obstruct the vertical or horizontal targets (**Figure 1**).

Experimental Protocol

The examiner would explain the protocol to the participant and subsequently obtain consent. Then the examiner instructs the participant to do three experiments:

Experiment 1. Eye Only Calibration

Examiner instructs the examinee to wear head-mounted laser and ensures the laser is on and pointed on the central target. The examiner would then use the custom timer for intervals that indicate the patient should move their eyes to the next target. This timer would begin with a 3 s count down, then a chime to begin the trial with a saccade to the left (5 degrees), then another 2 s, a chime to 10 degrees, and so forth until the patient reaches the limit of the horizontal plane. Next, the patient would return to the zero-degree target before proceeding in the opposite direction,

[1] About Face ID advanced Technology. *Learn How Face ID Helps Protect Your Information on Your iPhone and iPad Pro*. Apple Inc. Available: https://support.apple.com/en-us/HT208108 (accessed).

then repeat the process for the vertical plane. For our trial, we chose to begin by moving leftward in the horizontal plane, rightward in the horizontal plane then upward in the vertical plane, and downward in the vertical plane. We instructed the examinee to hold their eyes on that target until the next bell rings.

Experiment 2. Head Only Calibration

Repeat the process mentioned in Experiment 1, however, the head moves to the targets, while the eyes stay fixated on the central target. That is, the eyes move in the opposite direction of the head. In this experiment, the experimenter moved the head of the participant to reorient the laser toward the desired target so the participant could keep fixating on the central target.

Experiment 3. Head and Eye Calibration

Repeat the process mentioned in Experiment 1, however, the head and eyes move together to the targets. That is, the eyes do not move relative to the head. The experimenter moved the head of the participant to assist with simultaneous eye and head movements upon hearing the ring. Three of the twelve subjects moved the head without assistance.

Data Analysis

The data recorded through the application was exported securely to a cloud server for post-processing and data analysis. The analysis was done in MATLAB (The MathWorks Inc., Natick, MA, USA). Blinks, squints, and other well-understood intrusive artifacts in video oculography were automatically filtered out using data streams provided by Apple, which provide information about the face. To determine a zero position, we calculated the median eye/head position of the first 2 s of the test. This was needed because of the slight misalignment between the smartphone and the central target.

Subjects were asked to look at a new target every 2 s. To measure accuracy and precision, we only used the second half of those periods to allow time for the subject to move the head and/or the eyes and reach a new static eye and head position. **Figure 1** shows an example of complete recordings for horizontal eye position in Experiments 1–3.

RESULTS

We recorded eye movements from twelve volunteers, i.e., six women and six men, according to the methodology described previously. For each test, we calculated the accuracy and precision and plotted a chart to show the degree of error (accuracy) and the degree of variability (precision) from the true value. Across all experiments, the average percent error was 23% for eye position and 15% for head position while the precision was 1.3 degrees for eye position and 0.8 degrees for the head position. The error increased with the amplitude of the movement in all tests with an approximately linear relationship, so the percent error remained relatively constant across different positions.

Figure 2 shows the degree of error and variability in Experiment 1 when only the eye moved. The average percent error across all eccentricities was 33 $\pm$ 7% for horizontal eye position and 41 $\pm$ 8% for vertical eye position. The head tracking showed minimal error, accurately showing a stable head position near zero throughout the recording, 1 $\pm$ 0.2% for horizontal head position, and 0.2 $\pm$ 1% for vertical head position. The precision was 1.1 $\pm$ 0.2 degrees for eye position and 0.8 $\pm$ 0.3 degrees for head position with similar values for horizontal and vertical recordings in both cases.

Figure 3 shows the degree of error and variability in Experiment 2 when the head moved while the eyes kept fixating at the central and thus moving relative to the head. The average percent error across all eccentricities was 29 $\pm$ 3% for horizontal eye position, 34 $\pm$ 6% for vertical eye position, 23 $\pm$ 2% for horizontal head position, and 24 $\pm$ 4% for vertical head position. The precision was 1.4 $\pm$ 0.2 degrees for eye position and 1.2 $\pm$ 0.2 degrees for the head position with similar values for horizontal and vertical recordings in both cases.

Figure 4 shows the degree of error and variability in Experiment 3 when the head moved together with the eye so they both pointed toward the target and the eye did not move relative to the head. The average percent error across all eccentricities was 10 $\pm$ 10% for horizontal eye position, 7 $\pm$ 13% for vertical eye position, 21 $\pm$ 2% for horizontal head position, and 21 $\pm$ 2% for vertical head position. The precision was 1.7 $\pm$ 0.3 degrees for eye position and 1.6 $\pm$ 0.4 degrees for the head position with similar values for horizontal and vertical recordings in both cases.

DISCUSSION

Eye tracking enabled smartphones show great promise for the frontline assessment of eye movements in patients suffering from dizziness or other neurological disorders. In a recent study (12), we showed as proof of concept how using the application to perform the video Head-Impulse Test we could achieve a high correlation ($R = 0.8$) with measurements obtained with standard VOG devices. In this study, we focused on assessing more general metrics of data quality for eye and head position recordings. We found that the degree of error and variability increase in both eye and head movement as the eccentricity of targets increases. This is compatible with many other eye-tracking devices typically reported in the literature that have worse eye-tracking software performance as eccentricity gets larger (13). The application provided a more accurate measurement of head movements than eye movements, which we might expect due to its larger surface area and more landmarks for the smartphone to utilize when estimating where the head is facing. Also of note, the accuracy of both eye and head positions was better in the horizontal plane than in the vertical plane across tests.

Most eye trackers require a calibration before recordings. With ARKit's eye-tracking system, there is no declarative need for a calibration. Calibration is particularly useful for variations in data between individuals caused by eye shape, color, and overall compatibility with the eye-tracking software (14). Our data underscore that the smartphone shows a significant amount of error and variability between persons. We deduce then that a calibration protocol prior to testing may correct for the baseline error that each particular patient possesses. The protocol may

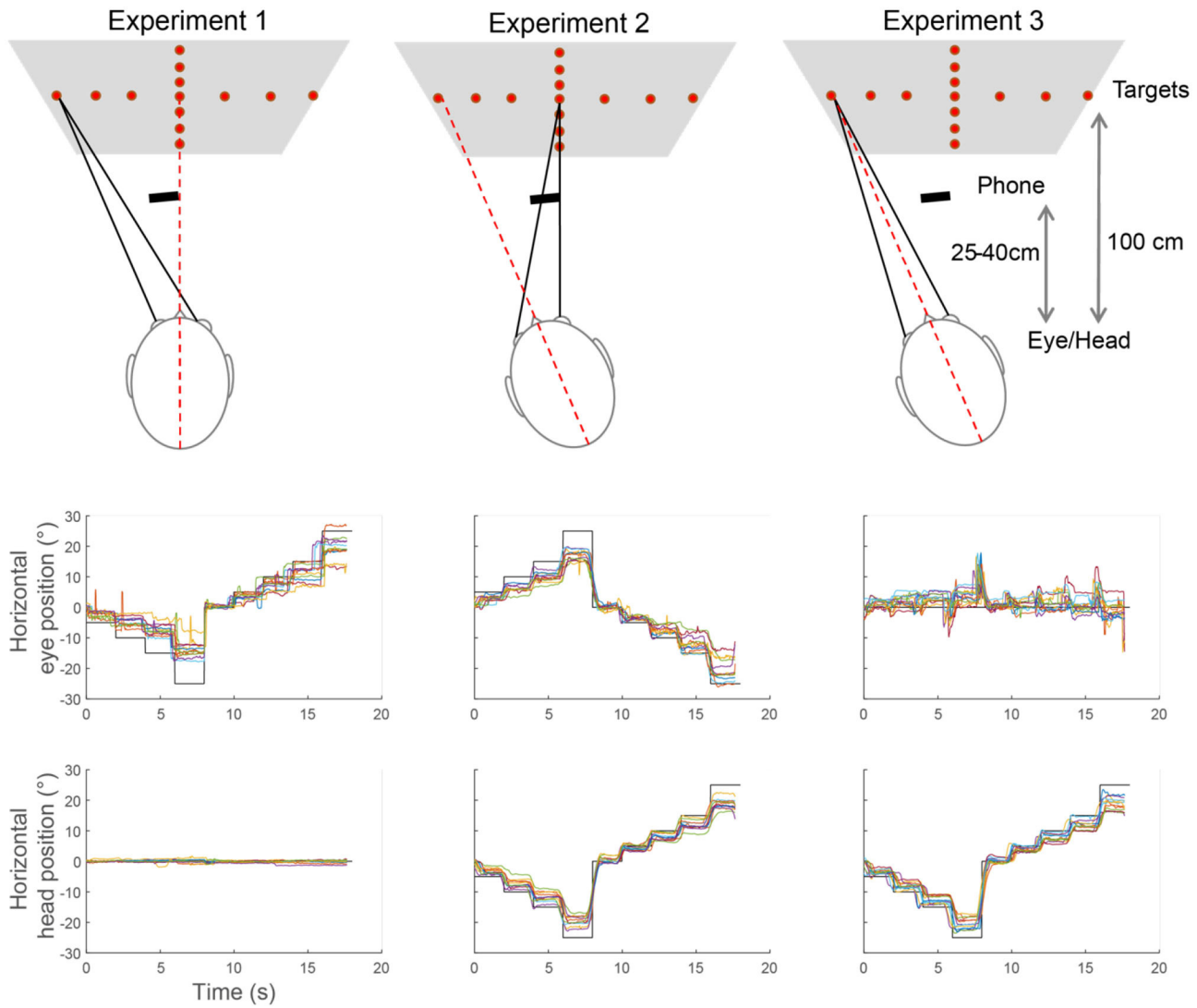

FIGURE 1 | Example of eye movement recordings during Experiments 1–3. The top row shows a description of the task in each experiment. The graphs below show, for each experiment, the position of the targets (black line), the eye, and head positions measured for each of the subjects (colored lines). Each step represents the eye or head moving to the next angle.

be similar to the methodology of the experiments described here. That is, having fixed targets on a wall at known distances that subjects are asked to look at sequentially. It may also be possible that applying a general correction to all recordings produces more accurate results without the need for a calibration procedure every time. This is the aim of future studies.

Future studies must also investigate the ideal conditions for data quality obtained with the smartphone application (i.e., optimum distance from the face, optimum lighting), existing documentation alludes to certain conditions such as holding the phone anywhere from 25 to 50 cm away from the face and even though the system works in the dark, those may not be the optimal conditions.

The metrics of ARKit's ability to quantify gaze while looking at the iPhone's screen has been explored recently, with accuracy reported in the 3.18 degree range (11). This study is most closely modeled by Experiment 1, however, they differ in that the patient is looking over the screen at a target on the wall 1 m away. We found that accuracy decreased with errors of up to 10 degrees for movements of 25 degrees. This difference leads us to suggest that data may be optimal when looking at the phone's screen but deteriorates as the eye looks further away as it may have been expected since the main objective of ARKit must be tracking the eyes while looking at the device.

The next step in optimizing smartphone performance in assessing eye and head movement is to devise what such a calibration protocol may look like and measure the improvement it produces. It is of particular significance for a protocol to calibrate according to the type of examination that is planning to be measured. For assessment of the dizzy patient with HINTS

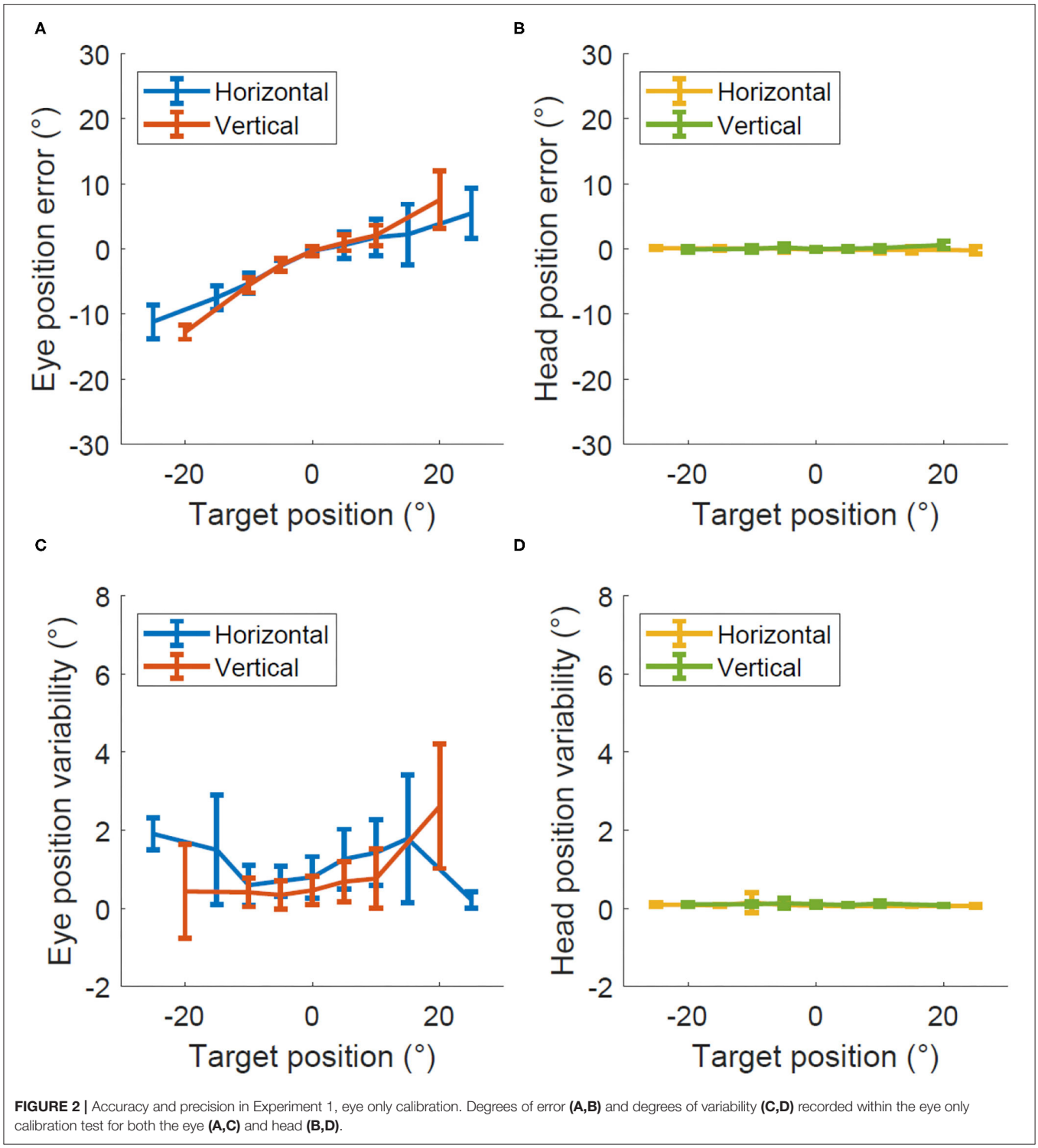

FIGURE 2 | Accuracy and precision in Experiment 1, eye only calibration. Degrees of error **(A,B)** and degrees of variability **(C,D)** recorded within the eye only calibration test for both the eye **(A,C)** and head **(B,D)**.

battery (Head Impulse test, Nystagmus, Test of Skew), it is imperative to make use of tests that can account for nystagmus, which can be intrusive in the context of other eye movements (4, 15). It may also be possible to develop protocols that are more robust to calibration errors, such as comparing the results of the head impulse test with baseline vestibulo-ocular reflex measurements at low speed. Our previous results (12) showed a good correlation between head impulse gain measured with the smartphone and with the clinical goggles but future studies should assess in a larger population the sensitivity and specificity of the head impulse and other tests and assess if additional calibration would be beneficial. Lastly, the protocol should be streamlined for speed and practicality, as these traits are valued in the urgent assessment of the dizzy patient when ruling out stroke.

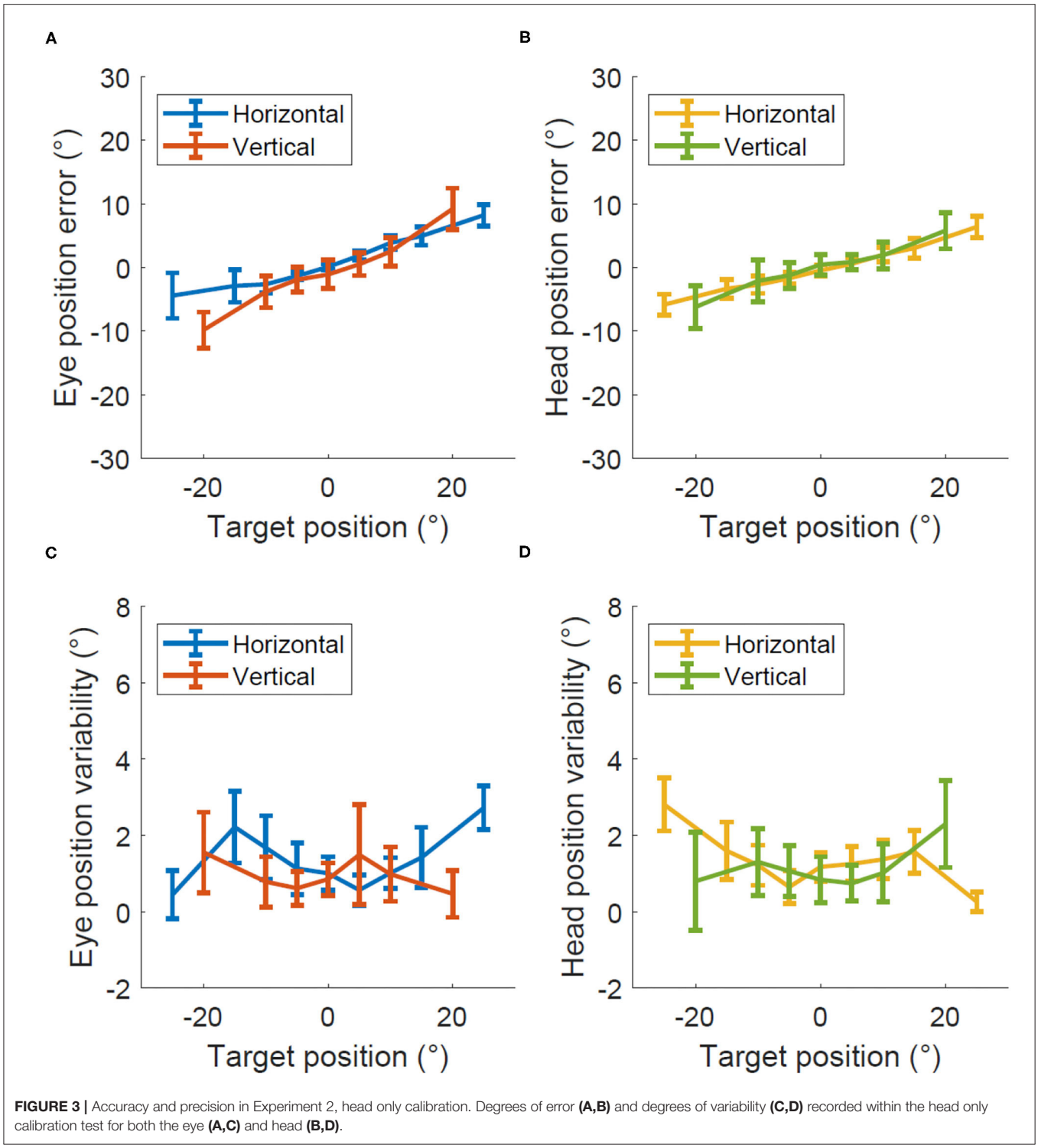

FIGURE 3 | Accuracy and precision in Experiment 2, head only calibration. Degrees of error **(A,B)** and degrees of variability **(C,D)** recorded within the head only calibration test for both the eye **(A,C)** and head **(B,D)**.

LIMITATIONS

It remains largely unknown how ARKit quantifies eye and head movements, and thus it is difficult to interpret the variabilities in our data between persons. Rather, we focus on the utility of the results in self-calibrating the phone to obtain the most accurate assessment of eye movements going forward when compared to reference standards. Considering that ARKit is designed for the user to look at the phone, rather than a distant target, we might expect poorer performance in eye tracking. However, applying calibration protocols prior to recording may eventually overcome the poorer performance. Moreover, we should note that this technology might not ultimately provide results as accurate as standard goggles but

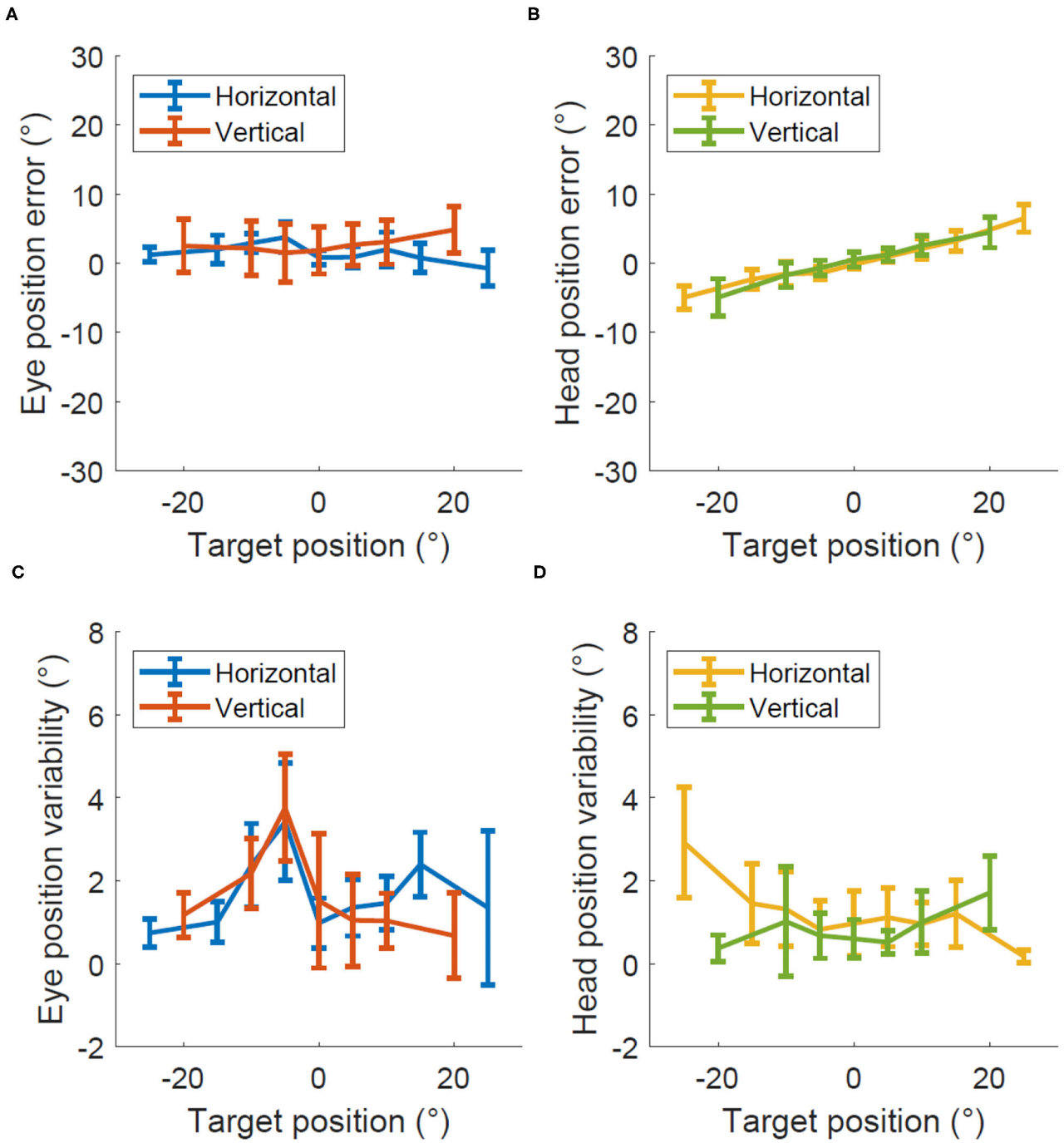

FIGURE 4 | Accuracy and precision in Experiment 2, eye and head calibration. Degrees of error **(A,B)** and degrees of variability **(C,D)** recorded within the eye and head calibration test for both the eye **(A,C)** and head **(B,D)**.

may be of value for places without access to those goggles. Another issue common to all eye-tracking system is the potential differences in data quality when recording people from different races and ethnicities. This is something that needs to be evaluated on a larger scale with more variety of races and facial profiles.

There are a wide variety of metrics we did not test on the smartphone. Some examples include accuracy of the facial coefficients (data streams providing information on whether someone has blinked, squinted, raised their eyebrows, and so forth), accuracy of large eye movements, accuracy at varying distances, lateral displacements, different facial features, lighting

arrangements, etc. There are a multitude of variables that can be explored to quantify their impact on the data and these will be a focus of future studies when determining the optimal environment for using the phone clinically.

CONCLUSIONS

The overall accuracy of the recordings made with a smartphone was lower than other commercial eye trackers. However, all the smartphone recordings were performed without a calibration protocol. Future studies should evaluate the utility of a calibration protocol when using smartphones to assess eye movements, specially, when the movements extend well-beyond the smartphone screen. Our metrics presented in this paper justify this potential need for calibration to achieve the optimal accuracy and precision that are crucial when measuring some pathologic eye movements. However, different tests may be affected differently by different qualities of the data. For example, low accuracy may not affect detection of catchup saccades or presence of nystagmus while low temporal resolution may affect detection of catchup saccades but not measurements of VOR gain or slow-phase velocity of nystagmus.

The new method may not replace at the moment the more accurate dedicated VOG devices. However, with the potential for further improvement in both accuracy and precision, this study represents a significant step toward the smartphone's deployment in the clinic providing a new and more accessible quantitative option for eye movement recordings.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Johns Hopkins University Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

TP, AH, AS, NF, DN-T, and JO-M have contributed to designing the study. TP, SB, and NF have contributed to drafting the manuscript. TP, NF, and JO-M have conducted statistical analyses. TP, SB, AS, NF, and JO-M have contributed to interpreting the findings. AH, AS, DN-T, and JO-M have critically revised the manuscript. All authors have approved the manuscript as submitted.

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The Power of Access in Parkinson's Disease Care: A Retrospective Review of Telehealth Uptake During the COVID-19 Pandemic

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Objective: The onset of the COVID-19 pandemic in March of 2020 forced a rapid pivot to telehealth and compelled a use-case experiment in specialty telehealth neurology movement disorders care. The aims of this study were to quantify the potential benefit of telehealth as an option to the Parkinson's disease community as shown by the first 9 months of the COVID-19 pandemic, and to quantify the potential impact of the absence of a deep brain stimulation (DBS) telehealth option on DBS patient follow-up.

Methods: New patient visits to the Inova Parkinson's and Movement Disorder's Center from April to December 2020 (9 months) were retrospectively reviewed for telehealth vs. in-person, demographics (age, gender, race, primary insurance), chief complaint, prior movement disorders specialist (MDS) consultation, imaging tests ordered, and distance/travel time from primary zip code to clinic. Additionally, DBS programming visit volume from April to December 2020 was compared to DBS programming visit volume from April to December 2019.

Results: Of the 1,097 new patients seen, 85% were via telehealth ($N = 932$) and 15% in person ($N = 165$). In the telehealth cohort, 97.75% had not consulted with an MDS before ($N = 911$), vs. 87.9% of in-person ($N = 145$). Age range was 61.8 +/– 17.9 years (telehealth), 68.8 +/– 16.0 years (in-person). Racial breakdown for telehealth was 60.7% White ($N = 566$), 10.4% Black ($N = 97$), 7.4% Asian ($N = 69$) and 4.5% Hispanic ($N = 42$); in-person was 70.9% White ($N = 117$), 5.5% Black ($N = 9$), 7.9% Asian ($N = 13$) and 5.5% Hispanic ($N = 9$). Top 5 consultation reasons, top 10 primary insurance providers and imaging studies ordered between the two cohorts were similar. Distance/travel time between primary zip code and clinic were 33.8 +/– 104.8 miles and 42.2 +/– 93.4 min (telehealth) vs. 38.1 +/– 114.7 miles and 44.1 +/– 97.6 min (in-person). DBS programming visits dropped 24.8% compared to the same period the year before (254 visits to 191 visits).

Conclusion: Telehealth-based new patient visits to a Movement Disorders Center appeared successful at increasing access to specialty care. The minimal difference in supporting data highlights the potential parity to in-person visits. With no telehealth option for DBS visits, a significant drop-off was seen in routine DBS management.

Keywords: telehealth, Parkinson's disease, movement disorders, specialty care access, DBS (deep brain stimulation), telemedicine (keywords), patient access, access to care

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INTRODUCTION

With the discovery and rapid proliferation of the coronavirus SARS-Cov-2 (COVID-19) in early 2020, medical care as a whole shifted rapidly to meet a changing landscape of patient needs. Inpatient and hospital-based clinical teams adapted to new safety requirements and an increase in both patient volume and acuity. At the same time, most outpatient clinics pivoted quickly to integrate a telehealth-based option into their workflow, balancing safety with access and continuity of care (1). This rapid change in the delivery of outpatient healthcare resulted in a shift whereby within a few weeks, the adoption of telehealth offset two-thirds of the decline in in-person clinical visits (2).

Prior to 2020, telehealth was viewed as a challenge for many older patients. In a 2018 study, 80% of older patients queried could successfully complete a telephone visit yet 38% reported being unable to successfully connect to a video visit (3). Reasons for this were broad and included such concerns as comfort with technology, physical or cognitive disability, privacy and IT security, telehealth platform design, internet connections and cost (3, 4). That said, the benefits of telehealth for access to care were already being established across medical disciplines, especially regarding the management of chronic conditions (5–9). Adoption of technology was also increasing in the 65 years and older population. One pre-pandemic Pew Research study reported roughly two-thirds of persons 65 years and older interacting with the internet, and smart phone ownership quadrupling in that age group in only 5 years. However, the same survey showed that 73% of persons over 65 reported needing help to set up or use a new device (10), thus reflecting increased access to technology but perhaps not a high level of comfort with those devices.

With the onset of the COVID-19 pandemic, the need for telehealth was no more acute than in Neurology clinics, specifically amongst Parkinson's and Movement Disorders specialty clinics. These patients are generally over the age of 65 and have chronic medical illnesses, putting them at a higher risk of hospitalization and poor outcomes from COVID-19 infection (11, 12). Furthermore, with the natural progression of Parkinson's disease (PD) and the absolute need for both longitudinal care and rehab services, delaying care due to poor clinical access or deferral of care had the potential to significantly set back the motor and non-motor function of many patients (12–15).

Prior studies had already established the viability of telehealth visits for Parkinson's disease patients, demonstrating positive patient and provider satisfaction as well as significant travel and cost savings for patients but no identifiable drop-off in quality of care nor outcomes (1, 16–19). One study showed that after completing a successful telehealth clinical visit, 80% of PD patients reported willingness to use telehealth again given the benefits of reduced travel time and improved access (20). This highlighted some of the known limitations of in-person specialty Parkinson's and Movement Disorders care: limited access, onerous burdens of the time and physical act of travel, as well as for many, the logistical challenges needed to schedule a clinical visit, travel to the visit then return home (19–21). Once the COVID-19 pandemic began, this was compounded by social limitations as well as patient's fears regarding the perceived safety of medical care and travel (22).

Born of necessity and with the above issues in mind, the Inova Parkinson's and Movement Disorders Center (IPMDC) pivoted quickly to offer telehealth visits to both new and follow-up patients starting in mid-March 2020. In-person visits were limited to a certain number per day, and initially only offered to patients requiring in-person procedures such as botulinum toxin injections and DBS adjustments. Very few clinical encounters were allowed to be scheduled face-to-face during the first few months of the pandemic due to local and national stay at home orders, limited to only very specific circumstances. Despite this the goals of clinical care remained unchanged: maintain patient-provider access to best manage the changes of a chronic, progressive medical condition, while navigating the disruption of the global pandemic.

IPMDC is a community-based Parkinson's and Movement Disorders Center, built within the integrated health network of the Inova Health System in Northern Virginia. At the time of the COVID-19 pandemic's onset, IPMDC was home to three fellowship-trained Parkinson's and Movement Disorders specialists running clinical care five days a week and in doing so, caring for a large and growing community of Parkinson's and other movement disorder patients.

This retrospective chart review study came about after the rapid and surprising uptake of new patient clinical appointments made after March 2020 to the IPMDC, where between the months of April and December, 1,097 new patients were evaluated with what seemed to be the vast majority having never consulted with an MDS before. Additionally, a drop-off of DBS follow-up visits was observed by the clinical team, presumably due to the necessity for an in-person visit to adjust the DBS system. Offering telehealth-based new patient appointments seemed to make engaging with an MDS possible for some who before believed it was not logistically an option, while the lack of a telehealth option appeared to limit access to a procedure-based clinical encounter such as a DBS programming. This is all within the context of the obvious early bias toward virtual visits during the beginning of the pandemic. Regardless, these circumstances allowed for a rapid test-case for offering telehealth services, and thus this retrospective chart review of the new patient appointments for the first nine months of the COVID-19 pandemic was done in an attempt to quantify the impact of telehealth on access to specialty care MDS.

MATERIALS AND METHODS

De-identified data was retrospectively collected from the 1,097 new patients seen by the IPMDC from April 1, 2020 to December 31, 2020 (first 9 months of the COVID-19 pandemic). A comparative univariate and multivariate analysis were then applied to the data using SAS statistical software. New patients aged 18 to 98 years old were included for analysis. Exclusion criteria were patient visits designated follow-up visits and visits completed before April 1, 2020 or after December 31, 2020.

The primary objectives were to gain a better picture of the degree of PD patients who gained first-time access to specialty care via the utilization of telehealth, compare the average distance which would have been traveled if the visits were in-person instead of telehealth, determine the degree of ancillary testing ordered via telehealth vs. in-person visits, and more. In collecting the data, there were charts which did not include one of the metrics identified; they were excluded from the calculation of that metric.

The secondary objective was to compare the frequency of DBS programming visits during the first 9 months of the COVID-19 pandemic with the same timeframe the year prior, with the goal of quantifying the potential impact of the absence of a telehealth option on the availability of clinical encounters for the DBS population.

The following data points were collected under a randomized patient identifier:

- Age
- Gender
- Race
- Zip code of patient's primary address
- Primary insurance provider for the patient
- Movement Disorders Specialist seen
- New patient visit date
- Visit type (telehealth or in-person)
- History of prior MDS consultation
- Primary reason for consultation
- Imaging tests ordered at this visit (MRI, CT, DaTscan)

Once collected, an Excel Driving Distance Calculator was used through Google Analytics to calculate the driving distance and low traffic travel time from the subject's primary zip code to the primary IPMDC clinic in Alexandria, VA.

A comparative univariate and multivariate analysis was then applied to some data using SAS statistical software, while others were presented as a simple comparison with percentages.

Regarding the secondary objective, the frequency of DBS programming visits during the first 9 months of the COVID-19 pandemic was compared with the same timeframe the year prior, with the goal of quantifying the potential impact of the absence of a telehealth option on the availability of clinical encounters for the DBS population. During the first nine months of the COVID-19 pandemic, DBS programming visits necessitated an in-person encounter. For this outcome measure, the inclusion criteria were age 18 to 98 years old and being designated a DBS programming visit (new and follow-up) conducted from April 1, 2020 to December 31, 2020. This was compared to a pre-pandemic cohort of DBS programming visits (new and follow-up) which were conducted from April 1, 2019 to December 31, 2019. To identify these patients, a deidentified count was made of clinical visits where the CPT code 95983 (denoting the first 15 min of DBS programming) was used during the timeframes above.

Telehealth visits were completed between the patient and the provider through Zoom, Doximity or Vidyo applications. A waiver of informed consent and a waiver of HIPAA authorization was granted for this retrospective chart review study.

RESULTS

During the first 9 months of the COVID-19 pandemic between April 1, 2020 and December 31, 2020, the Movement Disorders Specialists at the Inova Parkinson's and Movement Disorders Center saw 1,097 new patients. Of these new patients, 85% were conducted via a telehealth platform ($N = 932$), and 15% were conducted in-person ($N = 165$).

Only 2.25% of the telehealth-based visit cohort were documented to have seen an MDS before ($N = 21$), meaning 97.75% of the new patient telehealth-based visit cohort had never consulted with a specialist before ($N = 911$). When comparing this to the in-person new patient visit cohort, 12.1% were documented as having consulted with an MDS before ($N = 20$), with 87.9% having never consulted with a specialist before ($N = 145$) ($P < 0.0001$) (**Table 1**).

When noting the primary reasons for consultation with the IPMDC, the top diagnoses in both groups outside of not listed, were Tremor (24.8% of in-person vs. 21.6% of telehealth), Parkinson's disease (15.2% of in-person vs. 16.6% of telehealth), Memory Loss (6.7% of in-person vs. 7.5% of telehealth), Stroke (4.2% of in-person vs. 5.9% of telehealth), and Numbness (5.5% of in-person vs. 4.4% of telehealth). A proportion of new patient visits did not have a reason for referral or active referral form documented. As they were seen in a Parkinson's and Movement Disorders Center, the presumption is that most of those referrals were for MDS evaluation (**Table 2**).

Demographics and Insurance Coverage

Comparing the demographic breakdown of both cohorts, the telehealth-based cohort was 51% male ($N = 475$) while the in-person cohort was 47.3% male ($N = 78$) (P 0.3991). The average age for the telehealth-based cohort was 61.8 +/– 17.9 years (range 18 to 98 years old), while average age for the in-person cohort was 68.8 +/– 16.0 years (range 18 to 92 years) (P 0.0008) (**Table 1**).

Self-identified racial breakdown of the telehealth-based cohort were 60.7% White ($N = 566$), 10.4% Black ($N = 97$), 7.4% Asian ($N = 69$) and 4.5% Hispanic ($N = 42$). The in-person cohort was 70.9% White ($N = 117$), 5.5% Black ($N = 9$), 7.9% Asian ($N = 13$) and 5.5% Hispanic ($N = 9$). These top 4 racial designations accounted for 83.0% of the new patient telehealth-based visits ($N = 774$) and 89.7% of the new in-person visits ($N = 148$) (**Table 1**).

The top insurance provider in both cohorts was Medicare and Medicare MCO, accounting for a combined 41% of visits (39.5% of in-person vs. 50.9% of virtual). The next most common primary insurance providers for both cohorts were Medicaid and then Federal Blue Cross/Blue Shield (common in our area given the IPMDC's proximity to Washington, DC). All four of the top insurance plans are considered federal plans, and thus federal, non-private insurance plans make up 63.6% of the in-person new consultations and 57.3% of the virtual new consultations (**Table 3**).

TABLE 1 | Characteristics of virtual and in-person cohorts.

	Virtual ($N = 932$)		In-person ($N = 165$)		
Variable	**-**	**[min-max]**	**-**	**[min-max]**	***p*-value**
Male	475 (51.0%)		78 (47.3%)		0.399
Age	61.8 ± 17.9 (919)	[18–98]	66.8 ± 16.0 (165)	[18–92]	<0.001
Travel time (min)	42.2 ± 93.4 (923)	[5–1881]	44.1 ± 97.6 (165)	[5–1242]	0.812
Distance to Clinic (miles)	33.8 ± 104.8 (923)	[1.49–2120.65]	38.1 ± 114.7 (165)	[1.49–1406.71]	0.629
CT	19 (2.0%)		1 (0.6%)		0.341
MRI	221 (23.7%)		30 (18.2%)		0.132
DatScan	61 (6.5%)		11 (6.7%)		1.000
Seen MDS Before	21 (2.3%)		20 (12.1%)		<0.001
White	566 (60.7%)		117 (70.9%)		0.015
Black	97 (10.4%)		9 (5.5%)		0.046
Asian	69 (7.4%)		13 (7.9%)		0.872
Hispanic	42 (4.5%)		9 (5.5%)		0.550

TABLE 2 | Most common 5 diagnosis in both cohorts.

	Virtual		In-Person	
Ranking	**Diagnosis**	**N (%)**	**Diagnosis**	**N (%)**
1	Tremor	201 (21.6%)	Tremor	41 (24.8%)
2	Parkinson's	155 (16.6%)	Parkinson's	25 (15.2%)
3	Memory Loss	70 (7.5%)	Memory Loss	11 (6.7%)
4	Stroke	55 (5.9%)	Stroke	7 (4.2%)
5	Numbness	41 (4.4%)	Numbness	9 (5.5%)

TABLE 3 | Payer by visit type.

Primary payer	**Virtual N (%)**	**In-person N (%)**
MediCare	270 (29.0%)	65 (39.4%)
Medicare MCO	98 (10.5%)	19 (11.5%)
Medicaid HMO	85 (9.1%)	14 (8.5%)
FEP BCBS	81 (8.7%)	7 (4.2%)
United Healthcare	64 (6.9%)	8 (4.8%)
CIGNA	62 (6.7%)	12 (7.3%)
AETNA	61 (6.5%)	11 (6.7%)
N/A	52 (5.6%)	4 (2.4%)
Anthem	46 (4.9%)	7 (4.2%)
Carefirst	45 (4.8%)	8 (4.8%)

TABLE 4 | Imaging volume by visit type.

Imaging	**Virtual N (%)**	**In-person N (%)**
CT	19 (2.0%)	1 (0.6%)
MRI	221 (23.7%)	30 (18.2%)
DatScan	61 (6.5%)	11 (6.7%)

Imaging Tests, Distance Traveled and Volume Change Over Time

Comparing the imaging tests ordered during the new patient visit, more CT scans were ordered virtually (0.6% of in-person vs. 2.0% of telehealth, *P* 0.3415), slightly more MRI scans were ordered via telehealth (18.2% of in-person vs. 23.7% of telehealth, *P* 0.1317), and approximately the same number of DaTscan PET imaging were ordered (6.7% of in-person vs. 6.5% of telehealth, *P* 1.00) (**Table 4**).

Average driving distance that would have been traveled by the telehealth cohort (33.8 +/– 104.8 miles) was approximately the same as the distance traveled by the in-person cohort (38.1 +/– 114.7 miles), (*P* 0.6287). Low-traffic travel time was approximately the same, with the travel time of the telehealth cohort 42.2 +/– 93.4 min and the travel time of the in-person cohort 44.1 +/– 97.6 min (*P* 0.8117) (**Table 1**).

Over the course of the first 9 months of the pandemic from April 1, 2020 to December 31, 2020, the overall new patient volume (in-person and virtual) increased steadily from 81 new patients seen in April 2020 to a maximum of 170 new patients seen in October 2020. The number of patients who were seen in-person also increased steadily over the first 9 months of the pandemic, from 0 of the new patients seen in April 2020 to reaching its maximum of 43 in December 2020. Throughout, the majority of new patient visits were completed via telehealth, at minimum 81 a month and at maximum 141 a month (**Figure 1**).

Change in Face-to-Face DBS Programming Visits

DBS programming required an in-person encounter. Total IPMDC visits using CPT code 95983 from April 1, 2020 to December 31, 2020 were compared to the same visit type from April 1, 2019 to December 31, 2019. During the timeframe of April 1, 2019 to December 31, 2019, 254 such

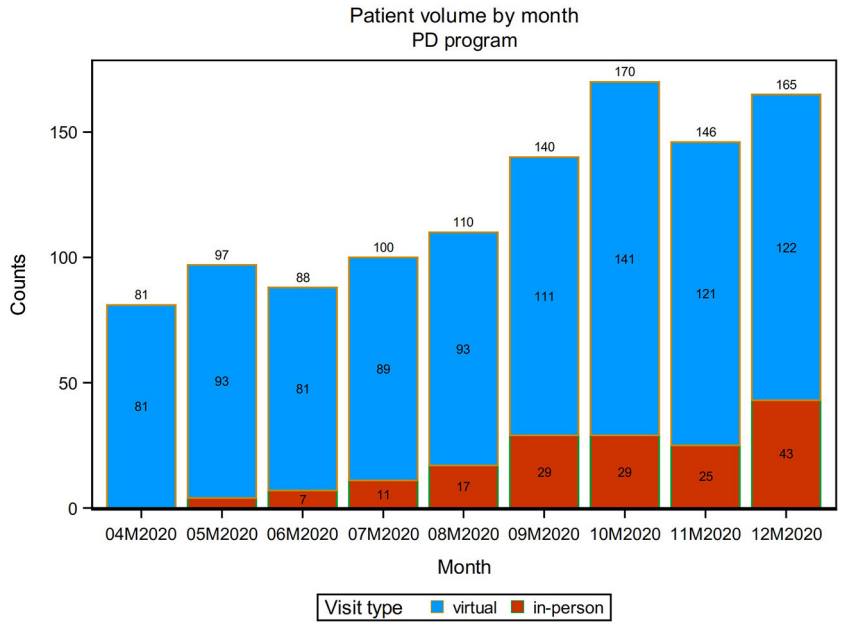

FIGURE 1 | Change in visit type from April 2020 (04M2020) to December 2020 (12M2020).

TABLE 5 | DBS clinical programming volume from April 1, 2019 to December 31, 2019 compared to April 1, 2020 to December 31, 2020.

Time frame	N
April 2019 to December 2019	254
April 2020 to December 2020	191

visits were conducted. During the same timeframe in 2020, denoting the first 9 months of the COVID-19 pandemic, 191 DBS programming visits were conducted, reflecting a 24.8% drop in DBS programming visits compared to the prior year (**Table 5**).

DISCUSSION

Prior to the onset of the COVID-19 pandemic in 2020, a discussion was already beginning within the movement disorders specialty regarding improving access for underserved populations using telehealth (1, 16–19). For years, the statistic that as few as 28% of Parkinson's disease patients were seeing an MDS has been seen as one of the many hurdles limiting the utilization of newly FDA-approved treatments (23).

Overall, neurology as a field suffers from variable density of neurologists throughout the US, and this access issue is enhanced when considering fellowship trained movement disorders specialists. One recent study showed that ∼20% of adult Medicare patients traveled outside of their hospital referral region for care with an average distance traveled of 148.7 miles. In this study, the most common neurological condition among patients who traveled outside of their home region was Parkinson's disease (24). That reflects only those patients who are able to travel. The limits of distance, logistics of travel, and time as well as physical and cognitive limitations keep many patients from seeking the highest level of care for their movement disorders diagnosis (25). These hurdles do not take into account the challenge of making a clinical appointment, even if travel were not an issue. On average in the U.S. wait time for a new patient visit with a Movement Disorder Specialist (MDS) is 2.2 months with a range of 2 to 8 months. Half of U.S. MDS Centers report a wait time longer than 2 months and approximately one-third of U.S. centers report wait times > 3 months (26). Without alternative solutions such as digital/telehealth options, many patients were more likely to delay or forego much needed care or simply believed that specialty care was unobtainable (22).

The onset of the COVID-19 pandemic in March of 2020 forced a rapid pivot to telehealth across the US, and at the same time, compelled a use-case experiment in specialty telehealth movement disorders care. At the IPMDC, this resulted in a significant increase in new patient visits starting in April of 2020 and continuing through at least the end of that year. Most new patient visits were completed via telehealth (85%) and the vast majority of those patients had never consulted with a specialty care MDS before (97.75%). This demonstrates how the offering of telehealth new patient visits created an opportunity for patients who before would not have been able to manage the logistics of an in-person visit related to mobility, distance, travel, and time. The increased uptake also suggests the upward trend of technology adoption in the 65-year-old-plus population likely also accelerated, as the number of new patient visits to the IPMDC via telehealth also increased over the first 9 months of the pandemic, hitting a high of 141 in October 2020.

There was a statistically significant difference in the average age of the two cohorts (61.8 years old virtual vs. 66 years old in-person, $P = 0.0008$), but not a significant difference in the travel time or distance between the patient and clinic (33.8 miles and 42.2 min virtually vs. 38.1 miles and 44.1 min in-person). This appears to highlight the universal utilization of telehealth visits across the age and distance spectrum, and the ability for those outside of the expected groups to capitalize on the logistical ease inherent to a telehealth visit. While telehealth visits may be most obviously beneficial for nursing home or assisted living patients, perhaps this shows an equal utility among younger patients who find it more convenient to log on to a virtual visit instead of taking significant time off work for an in-person visit. Or perhaps in general even those patients who could make an in-person visit simply preferred telehealth. This was exemplified by the continued high proportion of telehealth visits completed later in 2020 when in-person visits were more widely available. The universal appeal was also shown in the similarity in reasons for referral between the two cohorts, as the top 5 diagnoses offered were the same, reflecting little favoring of one diagnosis over another regarding a telehealth option. All of these factors reflect an increase in access to specialty Movement Disorders care—be it a prior limitation of distance or simply the logistics of a clinical visit irrespective of distance.

Most would expect a higher reliance on neuroimaging as a supplement to a reduced physical examination via a telehealth platform, and this data does show a higher rate of CT scans ordered via the telehealth cohort (2.0% vs. 0.6%), though noting the rare use of CT scan overall. MRI scans were ordered a slightly higher rate via telehealth at 23.7% vs. 18.2% and DaTscan PET imaging was also ordered at approximately the same rate between the two cohorts (6.5% telehealth vs. 6.7% in-person). This refutes the notion that telehealth necessitates higher reliance on neuroimaging, and in fact points toward relative parity between the workups initiated in-person vs. through a telehealth platform.

When evaluating the racial breakdown of the two cohorts, there appears to be little difference between the telehealth and in-person utilization of patients identifying as Asian or Hispanic, but those identifying as Black made up twice the percentage of virtual visits (10.4%) vs. in-person (5.5%). Black patients represent a traditionally underserved community within specialty Parkinson's disease care due to complex issues related to economic resources and insurance status as well as multifaceted organizational and social/cultural barriers (27). This two-fold increase in new patient visit utilization by Black patients suggests that telehealth may help alleviate some of the perceived barriers to seeking specialty care.

Regarding primary insurance coverage, the top 10 insurance providers were the same when comparing virtual new patient visits vs. in-person, with the top three in each Medicare/Medicare MCO, then Medicaid, then Federal Blue Cross/Blue Shield. When comparing the two groups, there was a 10% higher relative utilization of in-person visits compared to virtual visits within the Medicaire/Medicare MCO group (39.5% virtual vs. 50.9% in-person), but Federal BCBS patients favored telehealth by about two to one (8.7% vs. 4.2%). Perhaps this represents the preference for an in-person new patient visit for those over 65 who have Medicare, though noting the approximately 6 year average age difference between the two cohorts (61.8 +/– 17.9 years old telehealth vs. 68.8 +/– 16.0 years old in person).

When considering DBS patient visits, which prior to 2021 required an in-person visit to interrogate and program the DBS device, a 2020 study showed that 77% of DBS patients rely on another person for transport and 79% of DBS patients surveyed would see a more experienced DBS doctor, even out of state, if that doctor offered telehealth (28). This takes on different context when the median distance traveled to the nearest Movement Disorders specialty center for all patients is 56.1 miles, and even further for those in need to DBS management at 87.5 miles (29). Given the lack of a reliable telehealth-based DBS programming option in 2020, it comes as no surprise that the DBS programming visit volume at the IPMDC dropped by 24.8% compared to the same timeframe in 2019 (254 visits to 191 visits). Those that could forego their DBS adjustments did so during the first peak of the pandemic and *de novo* DBS implants were postponed in line with the early pandemic canceling of elective surgical cases. Ongoing studies related to telehealth DBS services, now FDA approved, will give a better picture of the utilization of a DBS telehealth option.

While this study suggests the benefits of telehealth regarding access, it bears noting the continued hurdles related to telehealth experienced by many. This includes access to reliable internet and technology, technical limitations of both hardware and software use, as well as for many the need for a care partner to successfully connect and complete a telehealth visit.

Finally, this data cannot be considered without pointing out the extenuating circumstances and limitations that were present regarding health market dynamics in the first nine months of the COVID-19 pandemic. At the beginning, all patients were shifted to a telehealth model or asked to delay their care. Though this mandate was loosened as the year went on, many patients continued to choose a telehealth option out of concern for safety as well as ease of access. While this is a known conflicting factor, future studies will hopefully help to quantify the impact that necessity had on telehealth uptake and help to delineate the role of telehealth on a potential volume and population-based increase in specialty care access. Additionally, the ideal metric on which to measure this data would be a comparison to pre-pandemic trends and percentage. This would represent a significant additional chart review which can be done in a follow-up study and was not possible within the framework and time dedicated to this study.

CONCLUSION

At the Inova Parkinson's and Movement Disorders Center, the forced experiment of telehealth new patient visits during the first 9 months of the COVID-19 pandemic was by all measures a success. Being able to reach MDS providers virtually without the logistical and physical hurdles of an in-person visit

allowed 911 of the telehealth-based new patients to consult with an MDS for the first time, representing 97.75% of the new telehealth-based patients. Additionally, the telehealth option resulted in twice as many Black new patient consults by percentage, possibly reflecting an avenue for increased access for a traditionally underserved community. Given the absence of a telehealth option for DBS programming visits, a significant drop-off (24.8%) was seen in visits involving routine DBS device management compared to the same timeframe in the pre-pandemic year before.

The minimal differences in age, gender, travel time and distance, chief complaint and imaging test utilization highlight the seemingly universal appeal of telehealth specialty services beyond simply the high-acuity and limited mobility patients. As more and more studies are published involving the parity of care and outcomes delivered via a telehealth model vs. a traditional in-person visit, this data aids that discussion, and suggests that the question should not be either/or, but simply how telehealth can continue to be an option that empowers patients with the benefits of moving beyond the hurdles of distance, travel, and time. If telehealth allows for greater and easier access to care of any type, including specialty care, and the percentage of Parkinson's patients able to partner with an MDS climbs beyond the current 28%, then the opportunity born out of a tragic scenario will have elevated our profession as a whole.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

SG and DF collected and organized data. DF wrote the main body of text. HW, DF, DW, SG, and SR provided editing. All authors contributed to the article and approved the submitted version.

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Remote Programming in Patients With Parkinson's Disease After Deep Brain Stimulation: Safe, Effective, and Economical

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Objective: The purpose of this study was to evaluate the safety, efficiency, and cost expenditure of remote programming in patients with Parkinson's disease (PD) after deep brain stimulation (DBS).

Methods: A total of 74 patients who underwent DBS at the Department of Neurosurgery, Zhongnan Hospital of Wuhan University between June 2018 and June 2020 were enrolled in this study. There were 27 patients in the remote programming group and 47 patients in the outpatient programming group. Clinical data, programming efficiency, adverse events, expenditure, and satisfaction were compared between the two groups.

Results: A total of 36 times of remote programming were performed on the 27 patients in the remote programming group, and four had mild adverse events during programming, and the adverse events disappeared within 1 week. The satisfaction questionnaire showed that 97.3% of the patients were satisfied with the surgical effect. The patients in the remote programming group (88.9%) were more likely to receive long-term programming after DBS than the patients in the outpatient programming group (74.5%). The Parkinsonism symptoms improved in both programming groups. The majority (18/27) of patients in the remote programming group lived away from the programming center, while the majority (27/47) of patients in the outpatient programming group lived in Wuhan, where the programming center was located ($P = 0.046$). The cost per patient per programming was US$ 43.5 in the remote programming group and $59.5 (56–82.7) in the outpatient programming group ($P < 0.001$). The median time cost for each visit was 30 min (25–30) in the remote programming group and 150 min (135–270.0) in the outpatient programming group ($P < 0.001$).

Conclusion: Remote programming is safe and effective after DBS in patients with Parkinson's disease. Moreover, it reduces expenditure and time costs for patients and achieves high satisfaction, particularly for patients living far from programming centers.

Keywords: Parkinson's disease, deep brain stimulation, remote programming, telemedicine, equipment safety, cost

INTRODUCTION

Parkinson's disease (PD) is a chronic neurodegenerative disorder characterized by motor and non-motor disabilities (1). Deep brain stimulation (DBS) is currently an effective treatment for advanced Parkinson's disease. However, patients will face long-term and repeated professional care after surgery, which is closely related to the clinical effect of surgery (2, 3). There are many barriers to implementing professional programming and care in outpatient clinics, including geographic and financial constraints, and patient's ability to travel (4, 5).

Telemedicine, which can remotely provide healthcare services using telecommunication technology to provide medical services to patients living in remote areas, has been used for care and evaluation of patients with PD (6–9). Remote programming is a new application of telemedicine that allows patients to receive adjustments in medications and parameters at home. DBS stimulators (G102, G102R, and G102RZ; PINS Medical, Ltd., Beijing, China) with remote programming capabilities have been in use in China since 2017 and have been successfully applied in VNS postoperative remote programming (10). Parameters can be programmed *via* a remote programming platform, on which physicians and patients can communicate *via* video chat, and physicians can adjust DBS parameters *via* an internet and Bluetooth connection. However, there is currently no evidence on the effectiveness and safety of remote programming after DBS in patients with PD. Since 2017, we have been applying this system for the postoperative programming of patients with PD after DBS. In this study, we analyzed the clinical data, programming effect, adverse events, programming cost, and patient satisfaction of 74 patients with PD who underwent postoperative remote or outpatient programming in our hospital.

METHODS

Patients and Grouping

Seventy-four patients who were implanted with a PINS DBS system (G102, G102R, or G102RZ) at the Department of Neurosurgery, Zhongnan Hospital of Wuhan University between June 2018 and June 2020 were enrolled in this study. The brain region targeted was the subthalamic nucleus (STN) of all patients. The diagnosis meets the diagnostic criteria of the British Parkinson's Society brain bank for primary PD (11). There were 27 patients in the remote programming group and 47 patients in the outpatient programming group according to the choice of patients and their families. The clinical data, programming effect, adverse events, programming cost, and patient satisfaction between the two groups were compared. The outpatient programming group was defined as each programming carried out in the outpatient department, and the remote programming group was defined as at least one programming performed through a remote programming system.

Remote Programming Procedure

The PINS remote programming system was adopted in this study. The remote programming center was located at Zhongnan Hospital of Wuhan University. The remote programming system mainly included a physician client (smartphone and computer), a patient client (smartphone), a patient programmer, and a server station (12). Before remote programming, the patients' family needed to download a PINS programming application (App, PINS "JiayiYoupin" patient version) to their smartphone and provide their personal information for verification. Through web service interfaces on the Internet, the server station built a virtual link between the physician client and the patient client. Programming procedure (**Figure 1**): (1) doctor would release programming permission in physician client (smartphone, PINS "JiayiYoupin" doctor version App); (2) patients should fill in the basic information and chief complaint and sign the remote programming agreement before they apply on the app, "JiayiYoupin" (**Figures 2A,B**); (3) a doctor would review and approve the application. During programming, patient's family should turn on the patient programmer, and keep the coil close to and connect with the implantable pulse generator (IPG) *via* near field wireless communication and connect it with the patient client through Bluetooth (**Figures 2C–E**); (4) the doctor communicated with the patient and their family members through the physician client and patient client by video chats on the Internet, and checked the patient's condition, and when the patient programmer was connected to the IPG, the doctor could check stimulation parameters, contact impedance, and battery voltage, and adjust stimulation parameters on the physician client under video monitoring, which included stimulation voltage, pulse width, frequency, and contacts, and, finally, observe a curative effect (**Figure 2F**); if necessary, the doctor could also adjust the amount of voltage, pulse width, and frequency on the patient programmer (**Figure 2F**); (5) after programming, the doctor would send the report to the patient client. If the network was interrupted during the adjustment, the system would automatically reset the last program parameters by default to avoid any harm to patients, and we would try to connect to the network again.

Data Collection

Clinical data were collected, including gender, age at DBS implantation, course of disease, preoperative Hoehn-Yahr stage, preoperative Modified Unified Parkinson's Disease Rating Scale III (MUPDRS III, drug-off) without rigidity and pullback test scores (13), and preoperative Levodopa Equivalent Daily Dose (LEDD). Also, we collected and analyzed the MUPDRS III score at the last follow-up (drug-off, stimulation-on), LEDD, time costs of each programming, distance from the patient's residence to the hospital, programming-related adverse events, and cost of each visit in the two groups.

We calculated the costs and time spent by the patients and families on the programming or visit in both groups. In the outpatient programming group, the costs included traveling costs, outpatient service costs for each visit, and working day salary lost by the family for accompanying the patient to the hospital. The time of outpatient programming was spent on traveling and programming. In the remote programming group, there was no other expenditure except for the fee of RMB 300 (US$ 43.5) that was charged for the remote programming, and time was spent on programming only. RMB was converted to US

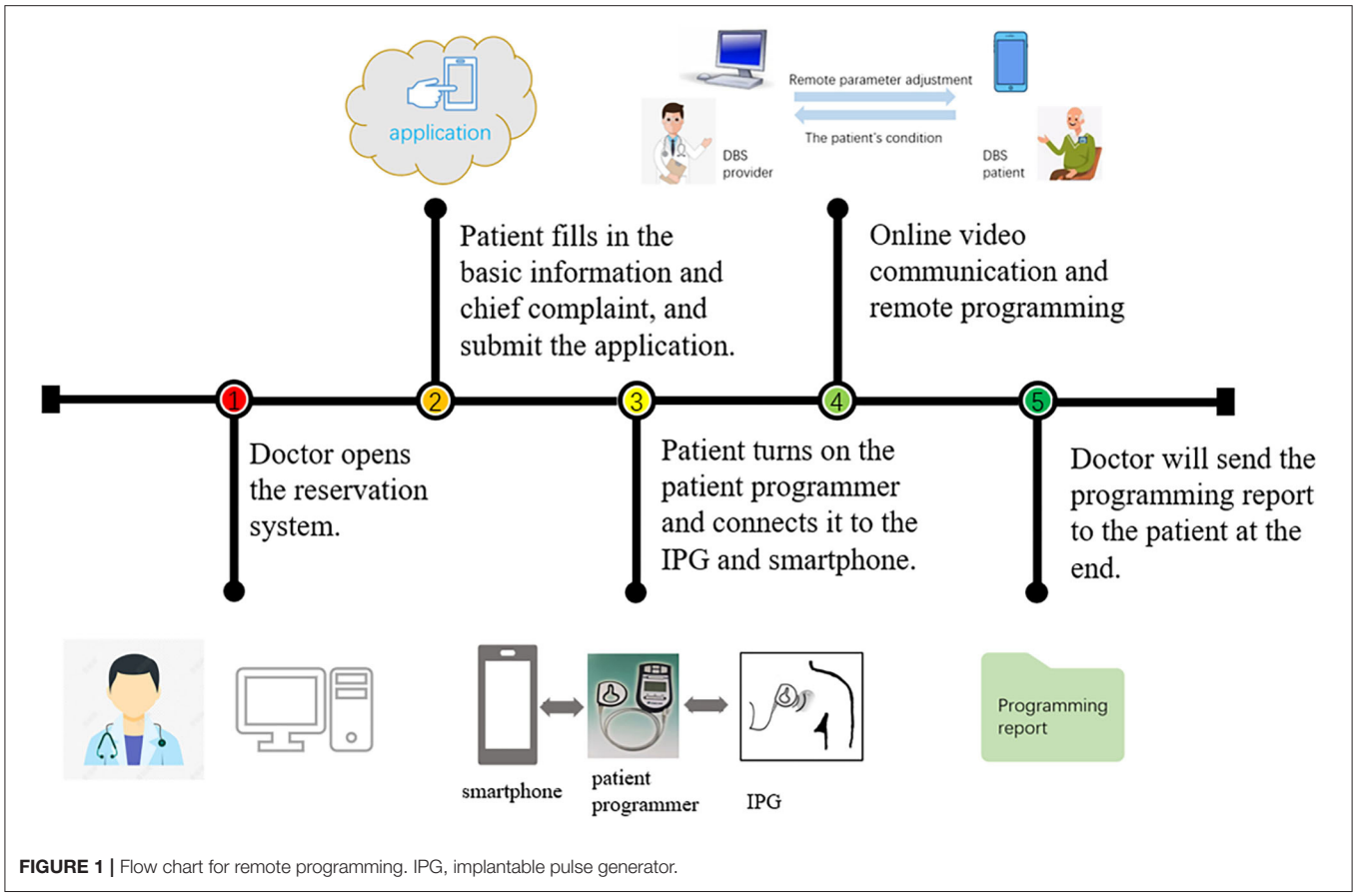

FIGURE 1 | Flow chart for remote programming. IPG, implantable pulse generator.

dollar according to the annual average exchange rate in 2019. The last follow-up date of this study was June 30, 2020.

Satisfaction Questionnaire

The scale of questionnaire was divided into two parts. The first part was about patients' satisfaction with the effect of DBS and willingness for long-term programming after surgery. The second part provided different questions for the two groups. The patients in the remote programming group were asked whether they were satisfied with the remote programming and reasons for satisfaction (open-type question). In the outpatient programming group, the patients were asked not only about their satisfaction with the outpatient programming but also their willingness for remote programming and reasons (open-type question).

Statistical Analysis

The SPSS 22.0 software was used for the statistical analysis of the data. An Independent sample *t*-test was conducted for continuous variables with normal distribution. Measurement data not conforming to normal distribution were expressed as median and 25th and 75th percentiles, and the Wilcoxon rank-sum test was conducted for comparison between the two groups. Count data were expressed by the number of cases, and the comparison between the groups was performed by the χ^2 test. *P*-value <0.05 was considered as a statistically significant difference.

Ethics and Informed Consent

The study was approved by the Medical Ethics Committee of Zhongnan Hospital of Wuhan University. Informed consent was obtained from the patients and their families.

RESULTS

Clinical Information of Patients

There were no significant differences in age, course of disease, preoperative LEDD and MUPDRS III score, and Hoehn-Yahr stage between the two groups. The MUPDRS III score and LEDD were improved at the last programming compared to that before the surgery in both groups, and there were no significant differences in improvements between the two groups. The distance from patients' residences to the hospital tended to be farther in the remote programming group. Further analysis of the residences of the two groups showed that most of the patients (18/27) in the remote programming group lived far away from Wuhan, and that most of the patients (27/47) in the outpatient programming group came from Wuhan where the hospital was located ($P = 0.046$, **Table 1**).

Remote Programming Contents

A total of 36 times of programming were performed for the 27 patients in the remote programming group, for which the

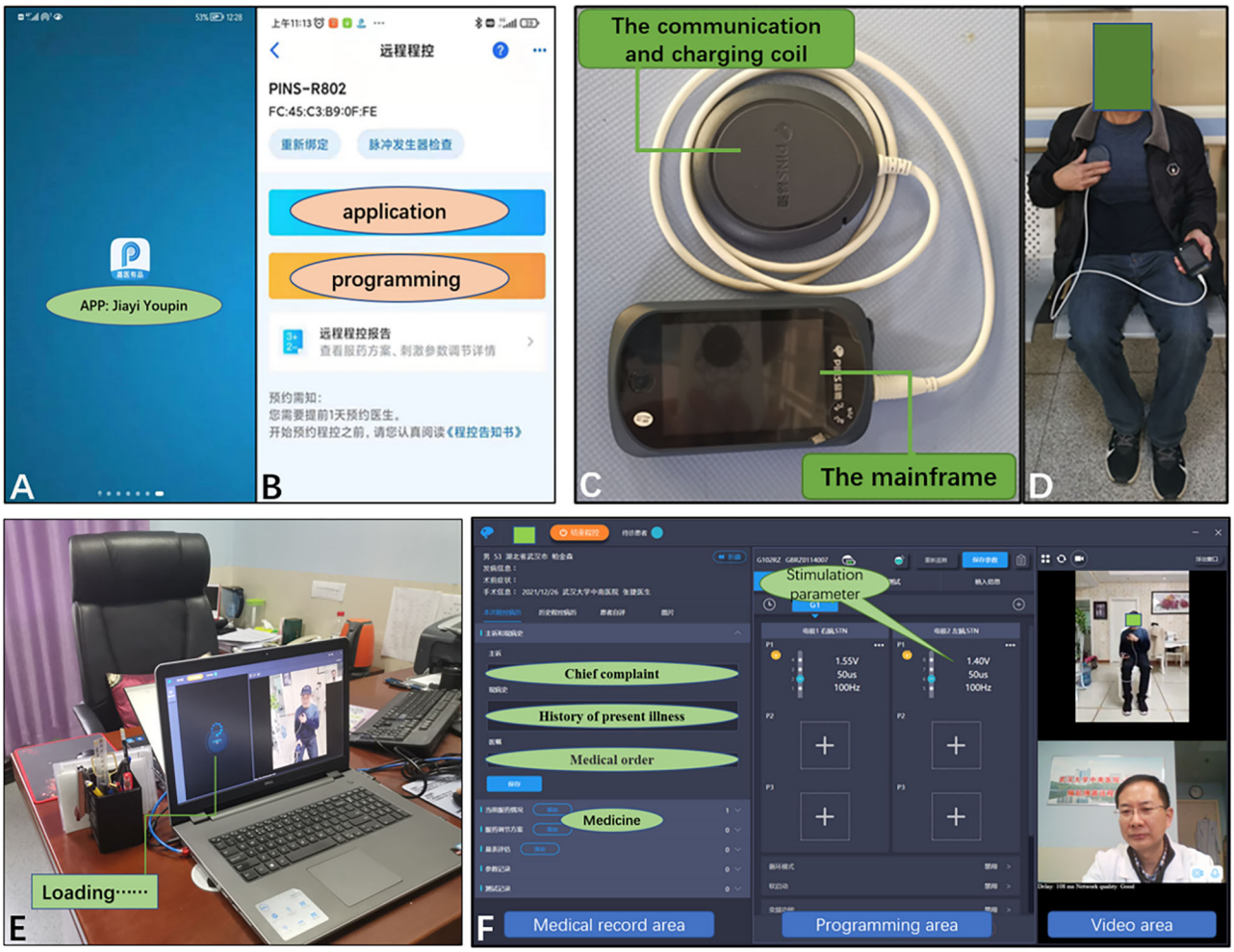

FIGURE 2 | (A) Patients needed to download the programming app, PINS "JiayiYoupin" patient version. **(B)** Patients applied for programming using the app. **(C)** The patient programmer consisted of a communication/charging coil and a mainframe, which can be used for programming and charging the IPG. **(D)** Working status of the patient programmer. **(E)** Doctor was detecting IPG signals in patient. **(F)** Computer interface of the physician client during remote programming, as well as the display of its functions. IPG, implantable pulse generator.

parameters were adjusted for 35 times, including 30 times of voltage adjustment, nine times of pulse width adjustment, 4 times of frequency adjustment, 10 times of contact adjustment, and six times of unipolar/bipolar adjustment. All the patients were assessed for battery voltage and contact impedance. Permission to adjust the parameter range was increased in 15 patients. Medicines were adjusted in 16 patients. Five patients were unable to raise the voltage by themselves because of limitation on voltage authority, resulting in poor symptom control, and it only took 15 min to adjust the voltage authority and improve the patient's symptoms by remote programming.

Adverse Events

Four (14.8%, 4/27) patients developed mild dyskinesia after programming in the remote programming group, including 3 cases of limb dyskinesia and 1 case of facial dyskinesia. Voltage was not lowered to improve the symptoms of Parkinsonism better, and dyskinesia was relieved within 1 week.

Satisfaction Questionnaire

The questionnaire showed that 97.3% (72/74) of the patients were satisfied with the surgical effect. There was a higher tendency in a desire to accept long-term programming after DBS in the remote programming group (88.9%) than in the outpatient programming group (74.5%). In the remote programming group, 85.2% (23/27) of the patients were satisfied with the remote programming because of it being convenient and economical, and less travel. In the outpatient group, 68.1% (32/47) of the patients were satisfied with the programming at the outpatient department, while 66% (31/47) of the patients were willing to try remote programming in the future, because it was convenient and economical. However, 34% (16/47) of the outpatients were

TABLE 1 | Clinical data between remote and outpatient programming group.

	Remote programming group $n = 27$	Outpatient Programming group $n = 47$	*P*
Gender (M/F)	15/12	21/26	0.368[a]
Age (years)	60.77 ± 0.6	61.16 ± 0.6	0.810[b]
Course of disease (years)	9.24 ± 0.2	12.17 ± 0.3	0.061[b]
Hoehn-Yahr stage (X ± S)	3.20 ± 0.7	3.40 ± 0.8	0.387[b]
Pre-op. LEDD (mg)	688.0 (450.0–825.0)	600.0 (400.0–831.0)	0.363[c]
Decrease rate of LEDD (%)[d]	46.0 (31.0–58.0)	33.0 (8.0–57.0)	0.368[c]
Pre-op. MUPDRS III (medicine-off)	29.0 (24.0–35.0)	32.0 (25.0–45.0)	0.157[c]
Improvement rate of MUPDRS III (%)[e]	64.02 ± 0.0	65.71 ± 7.5	0.692[b]
Distance from residence to programming center (km)	100.0 (14.0–228.0)	20.0 (15.0–150.0)	0.381[c]
Residence (Wuhan/other regions)	9/18	27/20	0.046[a]

*LEDD, Levodopa Equivalent Daily Dose; MUPDRS III, Modified Unified Parkinson's Disease Rating Scale III; [a] χ^2 test; [b] Independent sample t-test; [c] Wilcoxon rank-sum test; [d] (per-op. LEDD – LEDD at the last follow-up) / pre-op. LEDD * 100%; [e] (pre-op. MUPDRS III – MUPDRS III at the last follow-up) / per-op. MUPDRS III * 100%. MUPDRS III at the last follow-up was performed with medicine-off, stimulation-on.*

not interested in remote programming. The main reason was that residence was close to the programming center. Other reasons included difficulty of the procedure of remote programming to elderly people and complexity of patient conditions (**Table 2**).

Expenditure and Time-Cost Analysis

Thirty-six times of remote programming and 93 times of outpatient programming were performed. In the outpatient programming group, the cost of each visit was $59.5 (56–82.7), including $5.8 (2.3–29) for transportation, $10.2 for outpatient services, and $43.5 for absence from work, and was much lower in the remote programming group ($43.5 for programming, $P < 0.001$). In addition, the time cost for each programming was 30 min (25–30) in the remote programming group, while it was much longer in the outpatient programming group (150 min, 135–270, $P < 0.001$), most of which is cost of traveling (**Table 3**).

DISCUSSION

Safety, Effectiveness, and Economical Efficiency of Remote Programming

At present, DBS is an important treatment for movement disorders and involves continuous delivery of an electrical pulse through implanted electrodes connected to an IPG, and it is programmable in amplitude, pulse width, and frequency. The adjustment of stimulation parameters requires experienced clinicians and repeated visits to achieve maximum treatment benefit, which increased the burden for patients and their families. Therefore, tele-technology for remote programming was developed to solve this problem (14, 15). This study shows that remote programming can overcome geographical barriers between doctors and patients, and provide better medical services for patients economically and timely. Functions of traditional outpatient programming, including medical history collection, physical examination (MUPDRSIII), and parameters and medication adjustments, are also available for remote programming. In addition, patients are generally satisfied with this new technique, and only four cases of mild adverse reactions occurred but were gradually alleviated. It was very difficult for the patients to travel to the outpatient clinic by public transportation because of the restriction of Parkinson's disease on motor function. Almost all the patients needed family members to drive or reserve special vehicles to visit the hospital, which led to high travel expenditure. What is more, dates of outpatient programming were on working days, which led to loss of 1 or 2-day salary for families. On the contrary, the patients in the remote programming group only needed to afford the remote programming fee.

Satisfaction Questionnaire

The questionnaire showed that almost all the patients were satisfied with the surgical effect and long-term postoperative programming, and that remote programming had a higher satisfaction with advantages of overcoming restrictions in time and space, allowing the patients to make a programming appointment with their doctors timely and reducing the inconvenience of long-distance travel and financial pressure on the patients. Specifically, we asked the outpatients why they were not willing to try remote programming and found that most of them live near the programming center, which costs less and was relatively convenient. In general, the limitation of Parkinson's disease on patients' motor function makes all patients show a positive attitude toward a more convenient programming method.

Remote Programming Proposals

Similar to traditional programming, remote programming also follows the standard programming principle (16). Patients often require adjustment of parameters because of gait disturbance, rigidity, tremor, or speech disorder. Increasing voltage or pulse width, changing bipolar stimulation to unipolar stimulation or single contact to dual contact stimulation can improve gait disturbance and rigidity. Poor tremor control can be improved by higher contacts stimulating the zona incerta or changing

TABLE 2 | Satisfaction questionnaire results.

	Question	Range	Remote programming group $n = 27$	Outpatient programming group $n = 47$	Total	Testing value[a]	*P*	Remark
First part	Are you satisfied with the surgical effect of DBS?	Yes No	26 (96.3%) 1 (3.7%)	46(97.8%) 1 (2.1%)	72 (97.3%) 2 (2.7%)	0.242	0.623	
	Will you accept long-term programming after DBS?	Yes No	24 (88.9%) 3 (11.1%)	35(74.5%) 12 (25.5%)	59 (79.7%) 15 (20.3%)	1.598	0.206	
Second part	Remote group							
	Are you satisfied with remote programming?	Yes No	23 (85.2%) 4 (14.8%)					The reason for satisfaction: Economical; Convenient; Reducing the pain of travel; Timely solving problems
	Outpatient group							
	Are you satisfied with outpatient programming?	Yes No		32 (68.1%) 15 (31.9%)				
	Would you like to try remote programming?	Yes No		31 (66.0%) 16 (34.0%)				Reasons for willingness: Convenient, Economical. Reasons for unwillingness: The residence is located near PD Center; The procedure was difficult for the elderly; Patients' conditions were complex.

[a] χ^2 *value; PD, Parkinson's disease.*

TABLE 3 | Expenditure and time-cost for each programming in the remote and outpatient programming group.

	Remote programming group $n = 36$	Outpatient programming group $n = 93$	*P*
Programming time (min)	30.0 (25.0–30.0)	150.0 (135.0–270.0)	<0.001[a]
Total costs (US dollars)	43.5	59.5 (56.0–82.7)	<0.001[a]
Transportation fee	0	5.8 (2.3–29.0)	
Medical service fee	43.5	10.2	
Expense for absence from work	0	43.5	

[a] *z value.*

the single contact to double contact stimulation. Reducing pulse width or higher contact is helpful to speech disorder. In addition, medication can be properly adjusted according to patients' conditions. Attention should be paid to the following matters in remote programming: first, doctors should know each patient's stimulation targets, electrode depth and position, and main demands for programming; second, a wide range of adjustments, such as changing contacts or bipolar stimulation to unipolar stimulation, should be carefully carried out; third, when clinicians adjust the parameters, patients should sit safely to prevent falls; fourth, the authority of the patient programmer should be properly set within a safe range.

Dyskinesia

Because of inappropriate stimulation during programming, patients may experience symptoms, such as dysphonia, dizziness, and dyskinesia. For outpatients, we can observe and adjust timely, so adverse reactions during programming can be eliminated in the clinic. This procedure could not be carried out during remote programming limited by time and space. Therefore, in this study, we did not collect adverse reactions in the outpatient programming group. Dyskinesia was the only adverse reaction in the remote programming group, and was mainly manifested as involuntary movement and stereotype of limbs or the body after adjusting stimulation parameters or/and taking levodopa. The mechanism of dyskinesia is not completely clear. Studies suggest that dyskinesia is related to the long-term use of levodopa, and that about 40% of patients developed dyskinesia after 4 years of levodopa treatment (17–19). Although the dosage of the drug was significantly reduced after DBS, some patients may develop dyskinesia under the superposition of drugs and stimulation, especially for patients with preoperative drug-induced dyskinesia. Usually, stimulus-induced dyskinesia will gradually weaken or disappear after a few days or months. In

addition, dyskinesia can be alleviated or eliminated by changing the intensity of the stimulus, adjusting stimulation contact, choosing bipolar stimulation mode, or reducing the dose of dopaminergic drugs and changing the timing of medication.

Shortcoming of Remote Programming

Remote programming is not flawless. Clinicians cannot directly perform physical examinations on patients through video communication, which makes clinicians unable to know the patients' conditions very well. Therefore, remote programming cannot solve all problems for patients with complex conditions. Both doctors and patients should have a reasonable expectation on remote programming. If the patient's physical signs are transmitted in real-time in combination with wearable devices, it can partially make up for the lack of physical examination (20). In addition, equipment and network conditions can also affect the smooth progress of programming. Nevertheless, remote programming still has incomparable advantages over traditional programming and has broad application prospects. Especially, in the context of the coronavirus disease 2019 (COVID-19) pandemic, remote programming has become the ideal method for programming in patients with PD after DBS. With the application and popularization of the fifth-generation mobile communication technology (5G), remote programming will be further improved and will play an increasingly important role in postoperative programming for patients with PD.

CONCLUSION

Remote programming is safe and effective after DBS in patients with PD. Moreover, it reduces expenditure and time costs for patients and achieves high satisfaction, particularly for patients living far from programming centers.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Medical Ethics Committee of Zhongnan Hospital of Wuhan University. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

PN and JieZ contributed to the conception and design of the study. XY, YS, XZ, WL, and KF contributed to the acquisition and analysis of the data. PN, JibZ, and JieZ contributed to the drafting of the manuscript. All authors contributed to the article and approved the submitted version.

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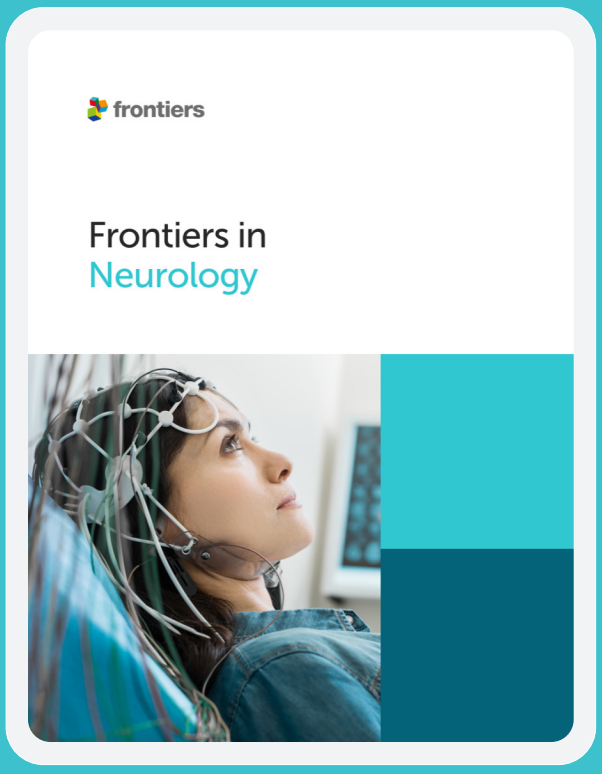

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